FROM

THE TRUSTEES AND FACULTY

OF THE

PEKING UNION MEDICAL COLLEGE

DEDICATION

PEKING UNION MEDICAL COLLEGE

1921

Staff and Students of Peking Union Medical College

This picture was taken in the forecourt of the Hospital. From left to right the groups are: nurses, administrative staff, faculty and hospital internes; to the right on steps, students; in background, laboratory assistants, hospital attendants, janitors, cleaners, cooks, laundrymen, gatekeepers, and other servants

Addresses & Papers

DEDICATION CEREMONIES

AND

MEDICAL CONFERENCE

PEKING UNION MEDICAL COLLEGE

SEPTEMBER 15–22, 1921

PEKING, CHINA
1922

* 1. Fh. 37.

RUMFORD PRESS
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PEKING UNION MEDICAL COLLEGE

OFFICERS AND BOARD OF TRUSTEES

1921

ADMINISTRATIVE OFFICERS IN PEKING

Director
Henry S. Houghton, M.D.

Superintendent of the Hospital
Ralph B. Seem, M.D.*

Assistant Superintendent of the Hospital
T. Dwight Sloan, M.D.

Dean of the Pre-Medical School
William Warren Stifler, Ph.D.

Superintendent of Nurses
Anna D. Wolf, A.M., R.N.

Comptroller
James S. Hogg

*On leave of absence from the University of Chicago.

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THE COLLEGE — HISTORY AND DESCRIPTION

BEGINNING OF THE WORK OF THE ROCKEFELLER FOUNDATION IN CHINA

The interest of the Rockefeller Foundation in China, shown so plainly in the establishment of this extensive medical center, is not new. As far back as 1908, the needs of the Far East had attracted Mr. Rockefeller's attention to such an extent that a commission was sent out composed of Dr. Ernest D. Burton and Dr. Thomas C. Chamberlin of the University of Chicago, to study the educational situation in China, Japan, and India. After spending several months in each country, this commission returned a report recommending the establishment at Peking of an educational institution for the teaching of the natural sciences. It was proposed, however, after consideration, to develop the branch of medical science only, rather than to undertake the more extensive program. Before any action was taken, a second commission was sent out in 1914, this time to China alone, to consider the needs and opportunities for medical work. This group was headed by President Harry Pratt Judson of the University of Chicago. The other members were Dr. Francis W. Peabody of the Harvard Medical School and Mr. Roger S. Greene, then Consul General at Hankow, later appointed Resident Director of the China Medical Board. Their report endorsed the suggestion that medical work be undertaken, and outlined a program for aiding medical schools and hospitals.

The China Medical Board was then formed as a branch of the Rockefeller Foundation. In the summer of 1915, a third commission was sent out, composed of Dr. William H. Welch of the Johns Hopkins Medical School, Dr. Simon Flexner of The Rockefeller Institute for Medical Research, Dr. Wallace Buttrick, Secretary of the General Education Board, and Dr. Frederick L. Gates of The Rockefeller Institute. This commission recommended the establishment of two medical schools, and studied in detail the opportunities presented in Peking and Shanghai. As a result, the decision was reached to enter into co-operation with the Peking Union Medical College, whereby the China Medical Board should take over the land and buildings on the basis of their original cost, and provide the maintenance and new construction costs.

ACTIVITIES OF THE CHINA MEDICAL BOARD

The purpose of the China Medical Board of the Rockefeller Foundation is to co-operate with other agencies in the gradual development of a system of scientific medicine in China. In other countries preventive work in medicine first engaged the main efforts of the Foundation, since the fostering of public health presents the prospect of far larger results in the welfare of nations and individuals, for the expenditure of any given sum, than an equal expenditure of effort and money on the treatment of the sick. In China, however, several factors have contributed to defer the initiation of direct activities in hygiene and preventive medicine by the Rockefeller Foundation.

In the first place systematic protection of the public health is properly a government function; and while private agencies can sometimes give valuable aid in such activities, their efforts are usually most effective when subordinated to a carefully conceived program of some governmental unit, such as a province or municipality. In the disturbed political conditions now prevailing throughout China, with frequent changes in the government, and with the authorities preoccupied as they are with other more pressing problems, the prospects for the early development of public health work on a large scale have not been encouraging. A second difficulty lies in the fact that confidence in scientific medicine is not sufficiently widespread to insure on the part of the people the co-operation necessary for the most effective work. Furthermore, it is clear that while much of preventive medicine as it is known in the West can be applied immediately in China, the conditions to be dealt with, whether biological, social, or economic, are so different from those in the West that it is important to precede any large effort in public health by a period of careful study of local conditions, in order that the measures undertaken may be properly adapted. Finally it must be admitted that a highly trained personnel is as necessary for a public health program as for the manning of hospitals, and that the number of doctors now available in China is not sufficient for any considerable extension of either kind of work.

The problem of medical education was therefore indicated as that which first demanded attention. With this in mind the following lines of activity have suggested themselves:

1. Pre-medical education, through strengthening of science courses in colleges.

2. Medical education.
   a. Undergraduate courses.
   b. Training of investigators, teachers, and clinical specialists through prolonged graduate courses and through practical work under proper guidance.
   c. Stimulating of private practitioners and missionary doctors, both foreign and Chinese, by short graduate courses.

3. Medical research, especially with reference to problems of the Far East.

4. Improvement of hospitals as training centers for internes and nurses, as models for imitation, as indispensable adjuncts to the practising physician, and as a means of popular education.

5. Diffusion among the Chinese people of a knowledge of modern medicine and public health.

6. Fostering of professional ethics through the development of character and ideals of service.

The most important contribution of the China Medical Board has been the reorganization of the Peking Union Medical College, which has included the gathering of a large staff of teachers, nurses, and administrative officers, recruited in part from institutions in the United States, Canada, and Great Britain, in part from among persons with considerable experience in medical missionary work in China, and now in increasing numbers from well-trained Chinese. The staff included in 1921 fifteen pre-medical teachers, fifty-seven teachers in the Medical School, thirty-one nurses, and forty-eight administrative and technical officers. Of these, one hundred and twenty-three are foreigners and twenty-three Chinese trained abroad. New medical school buildings, capable of accommodating classes of twenty-five, to be increased by some adjustments to fifty, and a 250-bed hospital, have just been finished and are now in use.

A Pre-Medical School with a three-year course, receiving middle school graduates with a good knowledge of English, has been estab-

lished to give the prospective medical students thorough preparation in physics, chemistry, biology, English, and Chinese. Students are also required to study either French or German during this period. The registration at the beginning of the school year 1920–21 was twenty-seven in the first year, twenty-three in the second, and nine in the third. The maintenance for the time being of this preparatory school has appeared to be a necessity, for although there are some colleges in China giving good courses in one or two of the sciences, some of the best institutions are very weak in these subjects, and none of them have thus far presented for admission to the Medical School students properly prepared in all three sciences. At the same time an attempt has been made to help other institutions to give better instruction in physics, chemistry, and biology. Direct grants have been made for this purpose to St. John's University, Fukien Christian University, Canton Christian College, and Yale-in-China, to be used towards both buildings and staff, while a small part of a grant to the Shantung Christian University Medical School has also been used for the pre-medical courses.

The Medical School proper of the Peking Union Medical College was opened in the fall of 1919, and there were last year thirteen students in the first and second year classes. The higher class began its clinical studies in the fall of 1921. Side by side with the undergraduate classes a number of Chinese and foreign doctors have been receiving instruction, some being admitted to regular undergraduate courses, a few attending special courses for graduates, and a larger number entering the clinics for practical work in the various departments. During the past twelve months there have been seventy-two such persons enrolled at different times, some of whom hold appointments as internes, residents, or assistants. The allowances paid for most of these positions are so much lower than those prevailing outside, even in mission institutions, that the educational significance of the service is clearly emphasized, and at the same time the danger is avoided of accustoming the young graduates to salaries larger than most of them could get elsewhere. For graduate students not holding regular appointments in the college the China Medical Board provides a limited number of fellowships, sufficient to cover tuition and maintenance, and in some cases also travelling expenses.

In a few cases very encouraging reports have been received as to the value of this graduate training, and now that the college has moved into its new quarters and has the larger part of its staff at work, it should be possible to render better service in this as in other branches of its activities. The special graduate courses for practitioners are being given mainly at the Chinese New Year and during the summer vacation.

A most important branch of the work of the College is the Nurses' Training School, which hopes to give to Chinese young women an education in nursing comparable to that offered in our best hospitals in the United States. Middle school graduation, or its equivalent, and a working knowledge of English are required for admission to the four-year course. The first year is devoted to work in the classroom and laboratory, and includes science courses in the Pre-Medical School. In the remaining years practical work in the wards is combined with instruction in theory. The aim is to turn out nurses who shall be prepared to take positions of responsibility in teaching and in other hospitals on an equality with nurses trained abroad. The fact that many institutions have been unable to secure foreign nurses, even when their support was assured, indicates the urgent need for Chinese of equal training, whose broad educational background will enable them to command the respect which the nursing department of a hospital must have if it is to play its proper part. Graduate students will be admitted also to the Nurses' Training School, and some of these, who have a good command of English, may be given scholarships for study abroad, if the quality of their work at the Peking school seems to justify the expense. Arrangements have recently been made with the women's department of Peking University for a combined course, the first years in the University and the latter part in the College Hospital, leading to the bachelor's degree in Peking University.

A Department of Dietetics has been organized and chemical studies of all important Chinese foods are being made, in order that hospital diets may be intelligently selected. Some instruction in dietetics is given to the pupil nurses, and informal courses have been arranged for others desiring to specialize in this subject.

While devoting its energies and its resources mainly to the Peking

school, the Board has been much interested also in the development of other institutions. In particular, grants have been made to the Hunan-Yale College of Medicine, and to the Shantung Christian University School of Medicine. Like the Peking school, the Yale school teaches in English, while Shantung University teaches in Chinese. Small grants have also been made to the Pennsylvania Medical School of St. John's University, and to the National Medical College, a Government school at Peking. The Hunan and Shantung schools have also been able to secure much more support than before from sources other than the China Medical Board, and though they still have many urgent needs, they have made such good use of their funds and have worked so constantly for higher standards that they should undoubtedly look forward to a future of great usefulness. Teachers from these schools on furlough have held junior teaching appointments in some of our best American medical schools, thus gaining useful experience and at the same time helping to win recognition for the institutions from which they come. In many cases the China Medical Board has given fellowships to teachers in medical schools other than the Peking school in order to enable them to carry on systematic study in their respective departments during their furlough years.

The medical profession of China has thus far labored under the serious handicap of not having any common language medium for scientific intercourse. There has been no generally accepted medical terminology in Chinese; and the groups trained abroad or in China under the influence of different foreign nationalities naturally cling to the language of their teachers, having no other satisfactory means of expression. At the instigation of the China Medical Missionary Association a joint terminology committee has been organized, which has now made great progress in preparing an official terminology for the medical and pre-medical sciences. Government institutions are now taking a leading part in the work, and the new terms are to be published with the sanction of the Ministry of Education. The China Medical Board has assisted in this enterprise and in the work of producing a medical literature in Chinese, through grants to the China Medical Missionary Association and the National Medical Association of China.

No especial institution devoted entirely to research has been contemplated, but it is expected that teachers in the medical schools will in time be able to make important original contributions to medical science, as it has been the intention in the Peking school to give the teachers some opportunity for such work. The China Medical Missionary Association also has a research committee with which the teachers at Peking co-operate. Through this organization it may be possible, by the co-ordination of the efforts of a wide circle of independent workers, to secure some results of value.

Much attention has been devoted to the raising of hospital standards in China, for the work of medical education may be largely wasted unless there are opportunities for young doctors to practice their profession under favorable circumstances. Similar waste is often observed in the case of Chinese with a highly technical training in other branches, who return to their native land to find no suitable employment in their specialties, and no older colleagues with long practical experience to give them the needed guidance. The leading position taken by the missionary societies in medical work in China has been recognized and the attempt has been made to co-operate with them by strengthening the hands of their doctors and nurses, thus conserving a most important force for medical progress. It was obviously impossible to co-operate effectively with all the three hundred or more medical mission centers in China, and the general policy has therefore been to aid those hospitals near the principal medical schools and to establish an intimate though wholly informal relationship between them and the schools. Preference has also been given to institutions located in important cities with good prospects of securing local support, and to those already possessing a good nucleus in staff, equipment, or buildings, as it was felt that in such cases the relatively small contributions which the China Medical Board could make would produce the largest results. The aid given has taken the form of contributions to the support of additional staff, to general maintenance expenses, and to improvements in buildings and equipment. Of late such contributions have not amounted to more than one-half of the total sum required for the proposed additions and improvements, the remainder being supplied by the missions. Up to June 30, 1921,

grants of this kind had been made to thirty mission hospitals and one purely Chinese institution. It is likely that the more urgent claims of strictly educational institutions will make it impossible hereafter to devote as large sums to this branch of the work as in the past. In any case the future development of these hospitals must depend mainly on their ability to enlist the support of the communities which they are trying to serve.

Not only have the mission contributions to these hospitals increased, but in many cases the improvements made have rendered it possible to secure added Chinese support. The China Medical Board has also given to a large number of doctors in mission hospital work, grants towards the cost of graduate study while they are on furlough. The great work that missionary doctors have done in the relief of immediate suffering speaks for itself and needs no further comment. While the ordinary mission hospital has many serious deficiencies, it has one great element of strength, not often shared by equally small institutions at home, in that it has the full time of one and sometimes of two or three experienced doctors devoted entirely to its interests, and the staff usually live so near the hospital that the patients have at least one resident physician constantly on call. One of the most important achievements of the mission hospital has been the creation of popular confidence in Western medicine, which has enabled the physician in times of epidemics to assist in the protection of the people far more effectively than he could otherwise have done. In places where there have been no hospitals, popular distrust has made effective campaigns against plague and other epidemics extremely difficult and often impossible. Appeals to mission doctors for help in such emergencies are constantly becoming more common, and their advice is frequently sought on matters of hygiene in local government institutions.

Up to the present time no separate effort has been made by the China Medical Board in the matter of popular education in public health matters. Much has been done by individual physicians, and by the China Medical Missionary Association in co-operation with other bodies, and in the future the medical schools will doubtless be able to assist materially.

While the China Medical Board has now been in existence nearly

seven years, it is still one of the youngest of the many foreign organizations at work in this country. Coming as it does into a well-prepared field and enjoying the friendly co-operation of so many who share the same interests, it hopes to make in time, with its growing experience, a helpful contribution to the progress of the great Chinese people.

HISTORY OF PEKING UNION MEDICAL COLLEGE

Medical missionary work in Peking commenced with the arrival of William Lockhart of the London Missionary Society in 1861. Previous to that time, Lockhart had worked in Macao, Shanghai, and Chusan. He opened a small dispensary and out-patient clinic near the British Legation, in Peking. After three years he was succeeded by Dr. Dudgeon, who for many years carried on a vigorous campaign directed toward the introduction of Western medicine into China. The work slowly progressed until the time of the Boxer rising, when all the buildings and the plant were destroyed.

After the Boxer rising, when the need for constructive and educational work on a broader basis was brought home to all the friends of China, the first attempt was made to establish a school of medicine on modern lines in Peking. In 1906, the London Missionary Society was joined by two others in the founding of a union school and shortly after, three other societies joined the Union, so that the missions concerned were six in number: the London Missionary Society, the American Board of Commissioners for Foreign Missions (Congregational), the American Presbyterian Board, the American Methodist Episcopal Board, the Society for the Propagation of the Gospel, and the Medical Missionary Association of London. The first class was graduated in 1911, just fifty years after the commencement of medical mission work by Dr. Lockhart in Peking.

This Union Medical College was the first medical college to be established in China by the combination of both British and American medical men, and through the co-operation of missionary societies representing different religious denominations. Its organizer was Dr. Thomas Cochrane of the London Missionary Society, who was fortunate in obtaining the patronage and financial support of the Empress Dowager, and many of the leading Chinese officials. He also received invaluable assistance from such men as the late Sir Robert Hart, Sir Ernest Satow, and Dr. Douglas Gray. Dr. Cochrane, whose home is now in London, was among the guests at the dedication ceremonies of the new buildings of the Peking Union Medical College, held in Peking, from September 15 to 22, 1921.

LOCKHART HALL, THE OLD UNION MEDICAL COLLEGE, NOW USED FOR THE PRE-MEDICAL SCHOOL

Main Entrance to the Medical School Group

Physiology Building, from the Auditorium

Private Patients' Building

The College was early recognized by the Chinese Government. The Board of Education gives a special diploma to all graduates and for some years certain government departments made annual grants towards the support of the institution. A very able group of men was secured as members of the teaching staff. Among these were the late Dr. H. V. Wenham, a man of exceptional charm and brilliant gifts, who came to China with the one aim in life of helping in the foundation of a modern medical school; Dr. J. G. Gibb and Dr. J. M. Stenhouse of England, and Dr. Francis J. Hall of America; all of them men to whom the cause of medical education in China owes a large debt of gratitude.

The teaching prior to the reorganization was in Chinese. Some of the graduates and students have distinguished themselves by public service in times of emergency. Two of the senior students laid down their lives for their country in the great plague epidemic in 1910, and during the Revolution of 1911 no fewer than thirty-two students were engaged in Red Cross work.

The College was slowly progressing, when in 1914 the Rockefeller Foundation despatched its commission to China to study the question of medical education there. As a final result the China Medical Board purchased the entire plant and arranged for the complete reorganization of the school under its present charter from the Regents of the University of the State of New York.

BUILDINGS OF PEKING UNION MEDICAL COLLEGE

The buildings of Peking Union Medical College and Hospital are located on San Tiao Hutung, between the Hatamen Ta Chieh and the Wang Fu Ching Ta Chieh, in the property known as the Yü Wang Fu, which comprises approximately ten acres of land. An attempt has been made to harmonize the buildings with the great architectural monuments of Peking by adopting as nearly as possible Chinese forms for the exteriors, with such modifications as were made necessary by the practical purposes for which the buildings were to be used. The most striking features of this treatment are the curved roofs of green tile, with conventional decorations of the eaves in colors, and the entrance courts designed after the model of the old temples and palaces. Fourteen buildings, designated by the letters of the alphabet from A to N inclusive, comprise the main group. Brief descriptions follow:

A. Auditorium: first floor — the auditorium with a seating capacity of 350 and an entrance hall for use as a social center; second floor — a social hall with serving room adjoining, and the offices of the Department of Religious and Social Work.

B. Anatomy Building: museum, classrooms, laboratories, and offices.

C. Chemistry Building: laboratories and classrooms, the Director's offices, the Library.

D. Physiology and Pharmacology Building: laboratories, lecture-rooms, offices.

E. Private Patients' Building: basement — European kitchens, stores, staff dining-room; first floor — office of Dietitian, living quarters of Assistant Dietitian, and certain other women members of the Hospital staff; second and third floors — rooms for private patients.

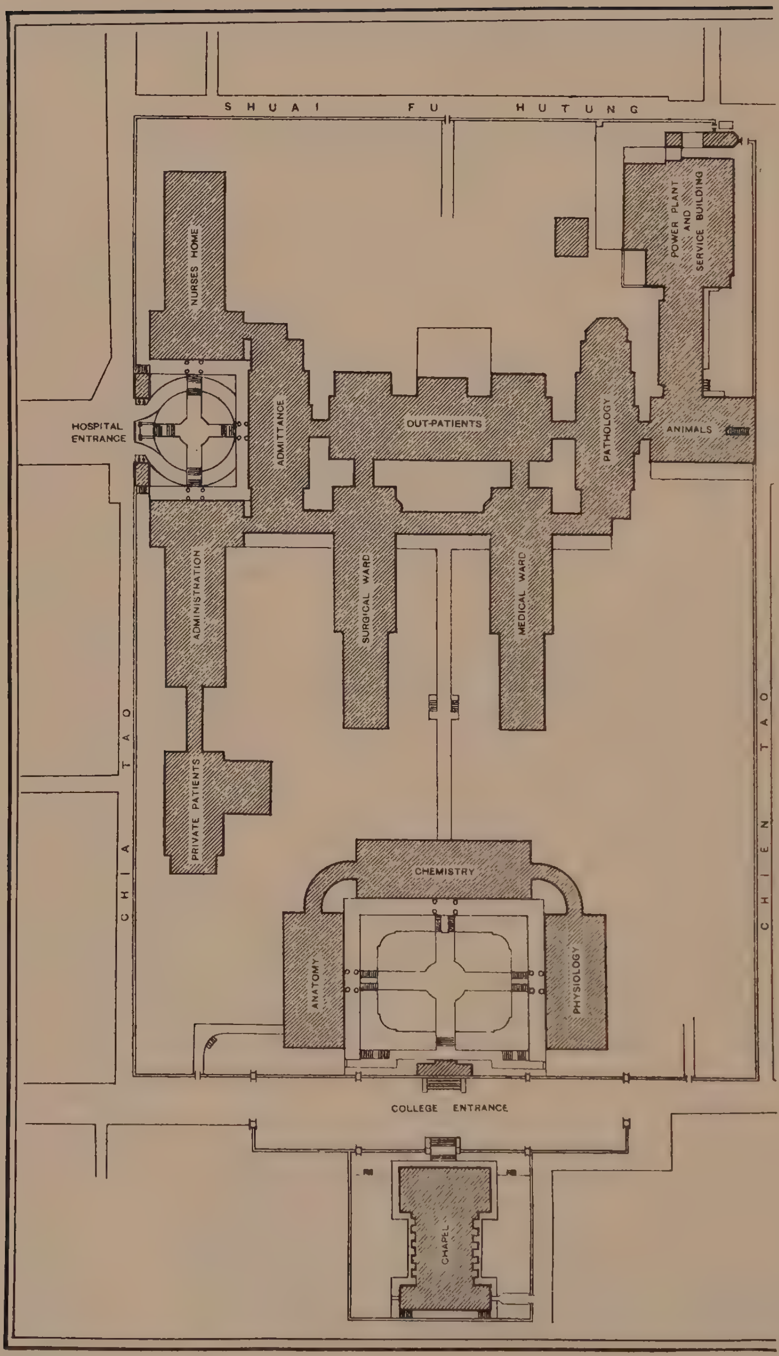
F. Administration Building: first floor — offices of the hospital administration; second floor — house officers' quarters.

G. Surgical Ward Building: three floors, each containing a twenty-five-bed unit; hospital supply storage in basement.

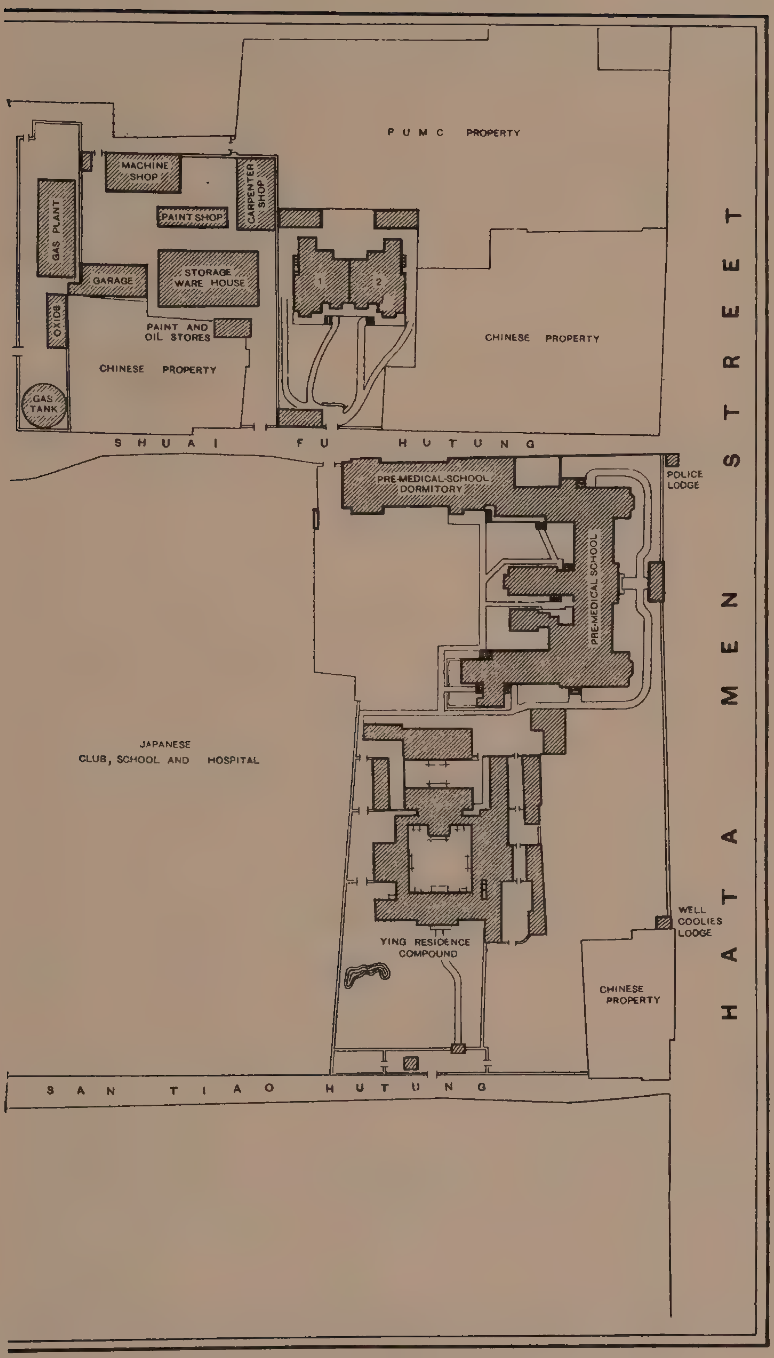
H. Medical Ward Building: three floors, each containing a twenty-five-bed unit; general stores in basement. Provision storage in corridor of basement.

I. Pathology Building: basement — autopsy suite, lecture-room, morgue, pathological specimen storage; first floor — Central Pathological Laboratory, Public Health, Parasitology, Museum, students' laboratory; second floor — laboratories of Bacteriology and Pathology, media supply division, research laboratories; third floor — laboratories of Chemical Pathology now used for study of Chinese foods, Department of Illustration and Photography, isolation ward for contagious diseases.

Second-Year Class in Physiology



General Plan of College Showing Location of College,



Hospital, and Pre-Medical School Buildings

Machine-Shop in the Physiology Building

J. Out-Patient Building: basement — kitchens for Chinese food, refrigerators, staff dining-rooms, out-patient clinics of Otolaryngology and Ophthalmology; first floor — out-patient clinics of Medicine and Surgery; second floor — Department of Roentgenology, laboratories for clinical diagnosis, classrooms and lecture-room for general use; third floor — clinical research laboratories and department offices; fourth floor — operating suites.

K. Admittance Building: basement — the Pharmacy workrooms, the admitting wards; first floor — Pharmacy, out-patient department admitting offices, out-patient clinics of the Departments of Obstetrics and Gynecology and of Pediatrics, clinical record-room; second and third floors — wards for Pediatrics, Orthopedics, Obstetrics and Gynecology.

L. Nurses' Home, including quarters for nurses, classrooms, and laboratories.

M. Power-House, including the laundry and quarters for domestics.

N. Animal House, offices of the Stores Department, including the receiving rooms.

Across a narrow street from the power-house are located the gas plant, machine shops, woodworking and paint shops, the garage, and a large storehouse.

Lockhart Hall, facing on Hatamen Street, houses the pre-medical departments: Biology, Chemistry, Physics, and Modern Languages, with their library. The Oliver Jones Dormitory, adjoining Lockhart Hall, has been used as the men's dormitory, but will in the autumn of 1922 become the dormitory for women students. When this change is made, the men students will take up quarters in the building formerly known as the Hsin Kai Lu Hospital, which is being remodeled for their use.

A picturesque group of Chinese houses in the Ying Compound is now used as quarters for the women students and three foreign women members of the staff.

Thirty-six residences, equipped with modern conveniences, have been provided for members of the staff, most of them grouped in two large enclosures known as the North and South Compounds, which are located within a few minutes' walk of the Medical School.

The total area developed for the use of the Peking Union Medical College, including the residence areas, is 22.6 acres.

MECHANICAL EQUIPMENT

There are four 250 horse-power Babcock and Wilcox boilers, equivalent to 1,000 horse-power, which supply steam power and heat throughout the institution.

The institution is furnished with light and power by three electric generators, with generating capacity of 375 kilowatts.

Distilled drinking water is furnished throughout the buildings.

Hot and cold water are supplied directly from the engine-room. A water-softening plant is being installed, as the local water is very hard.

Refrigeration and electrically controlled hot-rooms are distributed throughout the institution, and each laboratory is supplied with hot water, cold water, gas, compressed air, low and medium pressure steam, 110-volt direct current, 220-volt direct current, and in some laboratories 4-volt experimental current.

The institution has its own private telephone exchange with approximately 200 telephones in use, being connected with the outside switchboard by 10 trunk lines.

The hospital buildings are ventilated by means of electrically driven exhaust fans designed to change the air in each of the rooms from three to five times an hour, depending upon the speed of the fan.

Sewage systems have been provided for the entire institution. Sewage is pumped from the third section of the septic tank to the main city sewers by automatically controlled pumps.

Garbage and refuse are disposed of through an incinerator on the property.

The power laundry on the second floor of M Building is at present handling 3,000 pieces daily.

PROGRAM AND DELEGATES

PROGRAM OF THE MEDICAL CONFERENCE

THURSDAY, September 15, 1921

Morning

9–11 Registration

11:30–12:15 Address:

Salutatory. Dr. George E. de Schweinitz

Concerning the Evolution of Some of the Visual Phenomena of Pituitary Body Disorders. Dr. George E. de Schweinitz

Afternoon

2–5 Inspection of Plant

5–7 Reception and Tea

Evening

9–10 Address:

Medical Education in China: A Survey and Forecast. Dr. Edward H. Hume

FRIDAY, September 16, 1921

Morning

9:30–11 Clinical Sections:

General Medicine. Syphilis. Dr. H. Jocelyn Smyly

General Surgery. Operative Clinic: Radical Cure of Inguinal Hernia. Dr. Adrian S. Taylor

Obstetrics and Gynecology. Interesting Cases of the Year 1920–21. Dr. J. Preston Maxwell

Pathology. Present Day Aspects of Parasitology in China. Dr. Ernest C. Faust

Ophthalmology. Operative Clinic: Case 1. Extraction of Cataract; Case 2. Discission of Secondary Cataract. Dr. Harvey J. Howard

Otolaryngology. Operative Clinic: Esophagoscopy. Dr. A. M. Dunlap

11:30–12:15 Address:

Plague in the Orient with Special Reference to the Manchurian Outbreaks. Dr. Wu Lien Teh

Afternoon

2–5 Sightseeing:

Coal Hill and Pei Hai

Confucian and Lama Temples

Tung Yueh Taoist Temple

Evening

9–10 Addresses:

Medical Education in the Dutch East Indies. Dr. A. de Waart

An Adventure in Public Health. Dr. George E. Vincent

SATURDAY, September 17, 1921

Morning
9:30–11 Clinical Sections:
General Medicine. Symposium on Kala Azar. Dr. Oswald H. Robertson and Others
General Surgery. Demonstration: Balkan Frame and Apparatus for the Treatment of Fractures. Dr. George W. Van Gorder
Skin grafting—Thiersch and Reverdin. Dr. George Y. Char and Dr. Adrian S. Taylor
Obstetrics and Gynecology. Operation: Vaginal Cyst. Dr. John G. Clark
Demonstration: Case of Procidentia. Dr. John G. Clark
Pathology. Certain Aspects of Parasitology in the Philippines. Dr. Frank G. Haughwout
Ophthalmology. Presentation of Cases:
Case 1. Toxic Amblyopia. Dr. T. M. Li
Case 2. Quinine Amblyopia. Dr. Harvey J. Howard
Case 3. Chronic Iritis. Dr. T. M. Li
Case 4. Diminished Vision and Vitreous Opacities. Dr. Harvey J. Howard
Discussion. Dr. Harvey J. Howard, Dr. W. S. Thacker-Neville, and Dr. P. S. Soudakoff
Otolaryngology. Operative Clinic: Radical Mastoidectomy. Dr. J. Hua Liu

11:30–12:15 Address:
The Clinical Importance of the Vital Capacity of the Lungs. Dr. Francis W. Peabody

Afternoon
2–5 Reception at the President's Palace by President and Madame Hsü

Evening
9–10 Address:
Methods of Visualizing Modern Health Ideas (Illustrated by Motion Pictures). Dr. W. W. Peter

SUNDAY, September 18, 1921

Morning
10:30 Church Service:
Sermon by the Rt. Rev. L. H. Roots, D.D.

Evening
9–10 Organ recital. Mr. Ernest Hall
Program
Mélodie Religieuse — Henri Ravina
First Sonata — Mendelssohn
Allegro moderato e serioso
Adagio
Andante recitando
Allegro assai vivace

Prière et Berceuse	Guilmant
Tenor Solo from the Oratorio, "Elijah"	Mendelssohn
Recitative, "Ye people rend your hearts"	
Air, "If with all your hearts"	
Mr. D. W. Salisbury	
Prelude in C sharp minor	Rachmaninoff
Romance in D flat Andantino in D flat	Edwin H. Lemare
Offertoire	Lefebure-Wely

MONDAY, September 19, 1921

Morning
9:30–11 Clinical Sections:
General Medicine. Electrocardiography. Dr. Franklin C. McLean
General Surgery. Epithelioma. Dr. Frank Meleney
Discussion of Surgical Aspects of Epithelioma. Dr. Théodore Tuffier and Dr. Adrian S. Taylor
Obstetrics and Gynecology. Measurements of the Chinese Pelvis and the Main Forms of Contraction Seen in China. Dr. David E. Ford
Eclampsia and Eclampsism. Sir William J. Smyly, M. D.
Ophthalmology. Operative Clinic: Complete Tenotomy and Resection in Four Different Types of Strabismus. Dr. Harvey J. Howard and Dr. T. M. Li
Otolaryngology. Operative Clinic: Removal of Tonsils and Adenoids. Dr. A. M. Dunlap

Afternoon
4–5:30 Dedication Ceremonies:
Invocation. The Rev. J. Leighton Stuart, D.D.
Presentation of the Hospital and Medical School on Behalf of the Rockfeller Foundation. President George E. Vincent
Acceptance on Behalf of the College. Dr. Henry S. Houghton
Greetings on Behalf of the President of the Republic of China. His Excellency, W. W. Yen
Greetings on Behalf of the Ministry of the Interior. His Excellency, Chi Yao-san and Dr. S. P. Chen
Greetings on Behalf of the Ministry of Education. His Excellency, Ma Lin-yi
Response for the China Medical Board. Mr. Roger S. Greene
Response for the Rockefeller Foundation. Mr. John D. Rockefeller, Jr.

Evening
9–10 Address:
Biochemistry in Retrospect and in Prospect. Dr. A. B. Macallum

TUESDAY, September 20, 1921

Morning
9:30–11 Clinical Sections:
General Surgery. The Preparation and Use of Dakin's Solution. Dr. Adrian S. Taylor and Dr. Théodore Tuffier
Obstetrics and Gynecology. Causes of Uterine Hemorrhage. Dr. John G. Clark
Operation for Sterility. Dr. John G. Clark
Pathology. Conference on Pneumonic Plague. Plague Epidemic in the Chinese Eastern Railway Region in 1920–21. Dr. P. Lostchiloff and Dr. G. Tchaplik
Discussion. Dr. Wu Lien Teh, Dr. C. W. Young, and Dr. William H. Welch
Case Reports and Demonstrations. Case 1. Thrombosis of the Superior Petrosal Sinus and Meningitis, Following Acute Mastoiditis; Case 2. Syncytioma (Atypical Chorioma) of the Uterus, Terminated by Acute Peritonitis. Dr. Henry E. Meleney
Ophthalmology. Interesting Cases of 1920–21. Dr. Harvey J. Howard and Dr. T. M. Li
Neurology. Syphilis of the Nervous System. Dr. Andrew H. Woods

11:30–12:15 Address:
The Origin of Blood-Cells. Dr. Florence R. Sabin

Afternoon
2–5 Clinical Sections:
General Medicine. Conference on Leprosy. Dr. Victor G. Heiser and Others
Sightseeing:
Coal Hill and Pei Hai
Confucian and Lama Temples
Temples of Heaven and of Agriculture

Evening
9–10 Address:
The Search for the Ideal in Hospital Organization. Dr. S. S. Goldwater

WEDNESDAY, September 21, 1921

Morning
9:30–11 Clinical Sections:
General Surgery and Pathology. Tetanus. Dr. Adrian S. Taylor, Dr. Carl Ten Broeck, Dr. Johannes H. Bauer, and Others
Obstetrics and Gynecology. Maternity Famine Relief. Dr. Jean I. Dow
Demonstration of Woo's Needle. Dr. Arthur W. T. Woo
Ophthalmology. Operative Clinic: Three Cases of Expression for Trachoma. Dr. Harvey J. Howard and Dr. T. M. Li
Neurology. Syphilis of the Nervous System. Dr. Andrew H. Woods

11:30–12:15 Address:
Osteomyelitis. Dr. Théodore Tuffier

Afternoon
2–5 Clinical Sections:
General Medicine. Conference on Sprue. Dr. H. Jocelyn Smyly and Others.
Sightseeing:
Temples of Heaven and of Agriculture
Museum and Central Park
Lung Fo Ssu and Other Markets

Evening
9–10 Address:
Hookworm Control as a Promoter of Public Health Agencies. Dr. Victor G. Heiser

THURSDAY, September 22, 1921

Morning
9:30–11 Clinical Sections:
General Medicine. Tuberculosis. Dr. John H. Korns
General Surgery. Operative Clinic:
Case 1. Ankylosis of Hip. Dr. Théodore Tuffier
Case 2. Adenoma of Thyroid. Dr. Adrian S. Taylor
Obstetrics and Gynecology. Some Practical Aspects of Embryological Research in China. Dr. Paul H. Stevenson
Pathology. Pathological Problems in the Orient. Dr. William H. Welch
Ophthalmology. Presentation of Cases:
Case 1. Tuberculous Uveitis. Dr. Harvey J. Howard
Case 2. Primary Optic Atrophy. Dr. T. M. Li
Address: Some Newer Aspects of Uveal Tract Disorders and Therapeutic Measures for Their Relief. Dr. George E. de Schweinitz

11:30–12:15 Address:
The Present Status and Future Problems of Chemotherapy. Dr. Sahachiro Hata

Afternoon
2–5 Sightseeing:
Observatory and City Hall
Museum and Central Park
Western Hills and Pi Yun Ssu

Evening
9–10 Address:
Introduction of Dr. William H. Welch. General Leonard Wood, M.D.
The Advancement of Medicine and Its Contribution to Human Welfare. Dr. William H. Welch

ACADEMIC PROCESSION

September 19, 1921

Mr. John D. Rockefeller, Jr.
Mr. Roger S. Greene
Dr. S. P. Chen
His Excellency, Chi Yao-san
The Rev. J. Leighton Stuart
Sir Beilby Alston
Dr. William H. Welch
Dr. Paul Monroe
Mr. F. H. Hawkins
Dr. James L. Barton
Dr. J. A. Armitage
Mr. Edwin R. Embree
Dr. Francis W. Peabody
Dr. Thomas Cochrane
Dr. Victor G. Heiser
Dr. Robert T. Leiper
Dr. Sahachiro Hata
Dr. S. S. Goldwater
Dr. F. L. Hawks Pott
Dr. A. A. Gilman
Mrs. Lawrence Thurston
Dr. Edward H. Hume
Dr. Warren Stuart
Dr. E. W. Wallace
Dr. Peder N. Pedersen
Dr. Kuo Ping-Wen
Dr. P. C. King
Dr. Chang Po-Ling
Dr. Kenyon Butterfield
Dr. F. D. Gamewell
His Excellency, The Minister for Cuba
His Excellency, The Minister for Brazil
Bishop C. P. Scott
Bishop F. F. Keeney
Dr. C. C. Wong
Dr. D. E. Gossard
Dr. Frank G. Haughwout
Dr. Way-Sung New
Dr. Henry S. Houghton
His Excellency, W. W. Yen
Dr. W. T. Watt
His Excellency, Ma Lin-yi
Bishop F. L. Norris
Dr. Jacob Gould Schurmann
Dr. George E. Vincent
Mr. Martin A. Ryerson
Dr. R. M. Pearce
Dr. Frank Padelford (vice Dr. E. D. Burton, ill)
Sir William Brunyate
Dr. J. Christie Reid
Sir William J. Smyly
Dr. A. B. Macallum
Dr. Théodore Tuffier
Dr. A. de Waart
Dr. Florence R. Sabin
Dr. George E. de Schweinitz
Dr. A. J. Bowen
Dr. T. H. Lee
Dr. Mary Emma Woolley
Dr. Edwin R. Wheeler
Dr. F. F. Simpson
Dr. W. B. Nance
Mr. H. B. Graybill
Mr. E. C. Jones
Dr. John G. Clark
Dr. F. J. White
Dr. P. M. Roxby
Dr. William Fletcher Russell
His Excellency, The Minister for Norway
His Excellency, The Minister for Denmark
His Excellency, The Minister for Mexico
Bishop L. H. Roots
Dr. Antonio Sison
Miss M. K. Eggleston
Dr. Kenelm Digby
Dr. Wu Lien Teh

and the Faculty of the Peking Union Medical College

A Part of the Academic Procession at the Dedication Ceremonies

A Part of the Academic Procession at the Dedication Ceremonies

The Auditorium

A Group of Guests and Members of the Staff at the Dedication Exercises

OFFICIAL DELEGATES OF EDUCATIONAL AND SCIENTIFIC BODIES

Many organizations sent formal written greetings which were placed on exhibition in the buildings of the College. Only institutions which gave notification of the appointment of delegates are included in the following list.

American Medical Association
Dr. George E. de Schweinitz, President

American Presbyterian Board of Foreign Missions
Mr. T. H. P. Sailer

Batavia Medical School
Dr. A. de Waart, Director

Bureau of Science, Manila
Dr. Frank G. Haughwout, Director

Canton Christian College
Professor H. B. Graybill

Canton Hospital
Dr. W. Graham Reynolds, Chairman of the Board of Directors

Chinese Eastern Railway
Dr. P. Lostchiloff, Chief Surgeon
Dr. G. Tchaplik, Sanitary Division

Columbia University
Professor Paul Monroe

Fuh Tan University
Dr. Teng-Hua Lee, President

Fukien Christian College
Mr. E. C. Jones, President

Government of the Philippine Islands
Dr. Antonio Sison, Professor of Medicine, University of the Philippines

Ginling College
Mrs. Lawrence Thurston, President

Hangchow Christian College
Dr. Warren Stuart, President

Harvard University Medical School
Dr. Francis W. Peabody

Hongkong Medical Association
Dr. C. C. Wang, President

Hongkong University
Sir William Brunyate, Vice Chancellor
Dr. Kenelm Digby, Dean of the College of Medicine

Hunan-Yale Medical School
Professor Brownell Gage, Dean of the College of Arts
Dr. Edward H. Hume, Dean of the College of Medicine

International Health Board
Dr. Victor G. Heiser, Director for the East
Johns Hopkins Medical School
Dr. Florence R. Sabin
Johns Hopkins University
Dr. William H. Welch, Director of the School of Hygiene and Public Health
Kitasato Institute
Dr. Sahachiro Hata
McGill University
Dr. A. B. Macallum, Professor of Biochemistry
Mukden Medical College
Dr. Peder N. Pedersen
Dr. W. A. Young
Mt. Holyoke College for Women
Dr. Mary Emma Woolley, President
Nankai College
Mr. Chang Po-Ling, President
Nanking University
Dr. A. J. Bowen, President
National Medical Association of China
Dr. Wu Lien Teh
Dr. Way-Sung New, Secretary
Peking University
Dr. J. Leighton Stuart, President
London School of Tropical Medicine
Dr. Robert T. Leiper
Shanghai Baptist College
Dr. F. J. White, President
Shantung Christian University, Medical School
Dr. Edwin R. Wheeler, Acting Dean
Soochow University
Dr. W. B. Nance, President
Southeastern University
Dr. Ping-Wen Kuo, President
St. John's University
Dr. F. L. Hawks Pott, President
The Rockefeller Foundation
Mr. John D. Rockefeller, Jr., Chairman of the Board of Trustees
Dr. George E. Vincent, President
Tsinghua College
Dr. P. C. King, President
University of Chicago
Dr. Martin A. Ryerson, Chairman of the Board of Trustees
University of Iowa
Dr. William Fletcher Russell, Dean of the College of Education

University of Michigan Medical School
Dr. Ida Kahn
University of Paris and French Academy of Sciences
Dr. Théodore Tuffier
University of Pennsylvania
Dr. John G. Clark
Dr. George E. de Schweinitz
West China Union University
Dr. E. W. Wallace
Yale University
Mr. Edwin R. Embree

MEMBERS OF THE MEDICAL CONFERENCE

Peking, September 15-22, 1921

CANADA

Montreal
Dr. A. B. Macallum

CHINA

ANHWEI

Anking
Dr. Harry B. Taylor
Chaohsien
Dr. Charles A. Powell
Chuchow
Dr. E. I. Osgood
Hofei (Luchowfu)
Dr. Paul R. Tang
Dr. Frank Vierling
Hwaiyuen
Dr. H. Dabney Kerr
Wuhu
Mr. Charles O. Lee

CHEKIANG

Huchow
Dr. Fred P. Manget
Ningpo
Dr. S. H. Loo
Dr. Harold B. Thomas
Shaohsing
Dr. Claude H. Barlow
Dr. W. C. Sweet

CHIHLI

Kaichow
Dr. J. H. Brown
Kalgan
Dr. Harold Hammett
Dr. P. S. Shi
Dr. Woo Wai Yü
Nankou
Dr. C. S. Hsü
Paotingfu
Dr. Charles Lewis
Dr. Li
Dr. Maud A. Mackey
Miss Marie Rustin
Dr. Wang
Dr. J. Herman Wylie
Peking
Dr. T. Amano
Dr. K. A. Baird
Dr. Clementine Bash
Dr. H. Bonduel
Dr. J. A. Bussiere
Dr. P. Bykoff
Dr. H. Chambers
Dr. K. O. Chan
Dr. K. S. Chang
Dr. Y. N. Ch'ang
Dr. S. P. Chen
Dr. Tai-Ao Chen
Dr. Z. W. Chue
Dr. Bessie Coffin
Dr. Carl F. Coffman
Dr. J. G. Cormack
Major S. T. Dockray
Dr. P. M. Fairburn
Dr. Wu Jui Fang
Major Gillett
Dr. S. G. Kirkby-Gomes
Dr. Douglas Gray
Dr. Frances J. Heath
Dr. Myrtle J. Hinkhouse
Dr. N. D. Hopkins
Mr. C. K. Hou
Dr. H. C. Hou
Dr. E. T. Hsieh
Dr. J. H. Ingram
Dr. S. D. Joffick
Dr. K. Kamo
Dr. Matsutaro Kanno

Dr. Yamei Kin
Dr. T. E. Koo
Dr. P. Kuo
Dr. T. H. Lee
Dr. Y. T. Lee
Dr. Eliza E. Leonard
Dr. Ethel Leonard
Dr. George D. Lowry
Dr. Emma E. Martin
Dr. F. R. McDonald
Dr. E. Mercier
Dr. A. Monestier
Dr. W. B. Prentice
Dr. S. Ratkitin
Dr. Jean Redelsperger
Dr. Ho San
Dr. L. K. Sang
Dr. Lydia L. Schaum
Dr. Anne V. Scott
Dr. Arthur Shoemaker
Dr. Wu Tsen I. B. Sia
Dr. Spourgitis
Dr. E. J. Stuckey
Dr. C. C. Tang
Dr. Hugh W. Y. Taylor
Dr. Wu Lien Teh
(Harbin and Peking)
Dr. C. Chen Ting
Dr. Y. Tsching
Dr. Y. Y. Tsui
Dr. Susan Waddell
Dr. M. T. Wang
Dr. Pao-chen Wang
Dr. W. T. Watt
Dr. H. F. Wu
Dr. P. C. Wu
Dr. T. C. Yang
Dr. T. S. Yang
Dr. L. C. Yen
and 56 members of the staff of the Peking Union Medical College

Tientsin

Dr. Paul Bauer
Dr. J. W. Colbert
Dr. Woo Chi Fen
Dr. Pond M. Jee
Dr. H. Y. King
Dr. L. Howard King
Dr. Viola Lantz
Dr. P. K. Liang
Dr. E. Licent
Dr. Iva M. Miller
Dr. E. C. Peake
Dr. E. Robin
Dr. Li-Yuen Tsao
Dr. T. H. Wang
Dr. George S. Woodard
Dr. Marion Yang

Tunghsien

Dr. O. Houghton Love
Dr. Josephine M. Howard-Smith

Yungpingfu

Dr. John Kensall Robson

FUKIEN

Amoy

Dr. Edward J. Strick

Foochow

Dr. Jesse E. Gossard

Hinghwa

Dr. T. Y. Ling

HONAN

Changteh

Dr. Jean I. Dow
Dr. Percy C. Leslie

Chengchow

Dr. T. S. Sung

Hwaikingfu

Dr. W. Robert Reeds

Kioshan

Dr. Odd Eckfelt

Weihwei

Dr. R. G. Struthers

Wuan

Dr. F. F. Carr-Harris

Yencheng

Dr. H. C. James

HUNAN

Changsha

Dr. Reginald M. Atwater
Dr. John H. Foster

Dr. George Hadden
Dr. Edward H. Hume
Dr. Russell F. Maddern
Dr. Morris B. Sanders

HUPEH

Hankow
Dr. Hu Tsen Chiang
Dr. Takeo Ishikawa

Hanyang
Dr. Robert F. Francis

Wuchang
Dr. Mary Latimer James
Dr. Paul Wakefield

KIANGSI

Kiukiang
Dr. David C. Chang

Nanchang
Dr. George T. Blydenburgh
Dr. Ida Kahn

KIANGSU

Nanking
Dr. J. Y. T. Woo

Nantungchow
Dr. G. L. Hagman

Shanghai
Dr. Vivia B. Appleton
Dr. W. C. Dalbey
Dr. C. J. Davenport
Dr. Edward Foucret
Dr. Henry Fowler
Dr. J. Henry Gray
Dr. J. C. McCracken
Dr. Way-Sung New
Dr. W. W. Peter
Dr. A. C. Selmon
Dr. Bertha Loveland-Selmon
Dr. Phoebe Stone
Dr. A. W. Tucker
Dr. Sam Bell Wakefield
Dr. Clara B. Whitmore
Dr. Sien-Ming Woo

Soochow
Dr. K. H. Li

Wusih
Dr. Claude M. Lee
Dr. Y. L. Sz

Yangchow
Dr. Frances Cattell Ancell

KWANGTUNG (CANTON)

Canton
Dr. Charles C. Selden
Dr. Chee Iu Ting

Fatshan
Dr. Richard P. Hadden

Hongkong
Dr. Kenelm H. Digby
Dr. G. E. Thomas
Dr. C. C. Wang

Kongchuen
Dr. Edward W. Kirk

Swatow
Dr. Marguerite Everham

MANCHURIA

Changchun
Dr. Robert J. Gordon
Dr. Margaret E. McNeill

Chinchowfu
Dr. Sarah B. Keers

Dairen
Dr. M. Tsurumi

Harbin
Dr. P. Lostchiloff
Dr. G. Tchaplik

Hsiuyen
Dr. Viggo With

Lioyang
Dr. Isabella Aitkin

Mukden
Kate Drummond, R. N.
Dr. I. Inaba
Dr. W. S. Thacker-Neville
Dr. Peder N. Pedersen
Dr. Ethel L. Starmer
Dr. W. A. Young

Port Arthur
Dr. P. Kunisawa

Taheiho
Dr. Chia-Swee Lin

SHANSI

Fenchow
Dr. Percy T. Watson

Pingtingchow
Dr. Frederick J. Wampler

Taikuhsien
Dr. W. A. Hemingway

Taiyuen
Dr. Marjorie F. Edwards
Dr. E. H. Edwards

SHANTUNG

Chefoo
Dr. R. W. Dunlap
Dr. William Malcolm

Hwanhsien
Dr. Chü Pao Ch'in

Ichowfu
Dr. Emma E. Fleming
Dr. Benjamin M. Harding

Laichowfu
Dr. Jacob McF. Gaston

Lintsing
Dr. Paul V. Helliwell
Dr. Alma L. Cooke

Pingtu
Dr. George M. Herring

Taianfu
Dr. Waldo R. Oechsli

Tehchow
Dr. Lois Pendleton
Dr. Emma Boose Tucker
Dr. Francis F. Tucker

Tsinan
Dr. Samuel Cochran
Dr. J. Stanley Ellis
Dr. Philip S. Evans, Jr.
Dr. P. C. Kiang
Dr. T. C. Pa
Dr. Sawasaki
Dr. Thornton Stearns
Dr. E. B. Struthers
Dr. S. P. Tien
Dr. Edwin R. Wheeler

Tsingtao
Dr. M. Suzuki

Weihsien
Dr. E. W. Ewers

Yihsien
Dr. W. R. Cunningham

SHENSI

Sianfu
Dr. Alec A. Lees

SZECHUAN

Chengtu
Dr. Arnold Silcock
The Rev. Edward Wilson Wallace, B.D.

ENGLAND

Hastings
Dr. J. Auriol Armitage

London
Dr. Thomas Cochrane
Dr. Robert T. Leiper

FORMOSA

Tainan
Dr. James L. Maxwell

FRANCE

Paris
Dr. Théodore Tuffier

IRELAND

Dublin
Sir William J. Smyly, M.D.

JAPAN

Tokyo
- Dr. Kingo Goto
- Dr. Sahachiro Hata
- Dr. M. Inouye
- Dr. Mataro Nagayo
- Dr. Takeo Tamiya

JAVA

Batavia
- Dr. A. de Waart

KOREA (CHOSEN)

Chinju
- Dr. Charles I. McLaren

Seoul (Keijo)
- Dr. O. R. Avison
- Dr. K. Shiga
- Dr. Mary A. Stewart
- Dr. F. M. Stites

Shunshen (Gensan)
- Dr. P. L. Hill, Jr.
- Dr. J. B. Ross

Songdo
- Carrie Turner, R. N.

Oriental Consolidated Mines Hospital
- Dr. E. L. Power

UNITED STATES

Baltimore
- Dr. Florence R. Sabin
- Dr. William H. Welch

Boston
- Dr. Francis W. Peabody

Chicago
- Dr. R. B. Seem

Manila, Philippine Islands
- Major J. E. Ash, M. D.
- Dr. Frank G. Haughwout
- Dr. Antonia Guillermo Sison
- Governor General Leonard E. Wood, M. D.

New York City
- Dr. S. S. Goldwater
- Dr. Victor G. Heiser
- Dr. Richard M. Pearce

Philadelphia
- Dr. John G. Clark
- Dr. George E. de Schweinitz

Pittsburgh
- Dr. Hugh W. Bell
- Dr. F. F. Simpson

117 other persons, from China and abroad, attended sessions of the Conference.

CREDENTIALS OF DELEGATES AND MESSAGES OF FELICITATION

[THE PRESIDENT AND FELLOWS OF HARVARD COLLEGE TO THE FACULTY AND TRUSTEES OF THE PEKING UNION MEDICAL COLLEGE]

GREETING:

Harvard University sends its congratulations to the Peking Union Medical College upon the Dedication of its Building, at Peking, China.

Gladly availing themselves of the invitation to be represented at the ceremonies and at the Medical Conference, September fifteenth to twenty-second, nineteen hundred and twenty-one, the President and Fellows of Harvard College have appointed Francis Weld Peabody, A.B., M.D., Associate Professor of Medicine, as their delegate and have charged him to convey their felicitations.

Given at Cambridge on the twenty-third day of June, in the year of Our Lord the nineteen hundred and twenty-first, and of Harvard College the two hundred and eighty-fifth.

(Signed) A. LAWRENCE LOWELL
President

(Seal)

[UNIVERSITY OF PENNSYLVANIA]

June 2nd, 1921

THESE LETTERS

are to designate and appoint our loyal alumnus
GEORGE EDMUND DE SCHWEINITZ, A.M., M.D., LL.D.,
Professor of Opthalmology
as our official delegate to represent
THE UNIVERSITY OF PENNSYLVANIA
at the dedication of the Building of the
PEKING UNION MEDICAL COLLEGE

and at the Medical Conference to be held in Peking, China, from September the fifteenth to the twenty-second, nineteen hundred and

twenty-one, and to convey through him in person the felicitations and high regards of this University to the Faculty and Trustees of the College.

(Signed) Josiah H. Penniman
Acting Provost
(Signed) E. W. Mumford
Secretary

(Seal)

[American Medical Association to the Director and Trustees of the Peking Union Medical College]

Greeting:

The Board of Trustees of the American Medical Association has designated the President-Elect of the Association, Dr. George E. de Schweinitz of Philadelphia, State of Pennsylvania, United States of America, to convey to the Director and Trustees of the Peking Union Medical College the congratulations and salutations of the American Medical Association on the occasion of the dedication of the new buildings of the Peking Union Medical College and the inauguration of its new Director, Dr. Henry S. Houghton.

Issued under the seal of the Association at the office of the Secretary in the City of Chicago, Illinois, U. S. A., this twelfth day of July, A.D. 1921.

(Signed) Hubert Work
President
Attest
(Signed) Alex. R. Craig
Secretary

(Seal)

[University of Iowa]

The University of Iowa extends its sincere felicitations to the Faculty and Trustees of The Peking Union Medical College of China upon the dedication of the new hospital and laboratory buildings and upon the inauguration of Doctor Henry Spencer Houghton as new director September fifteenth nineteen twenty-one bespeaking for that most illustrious institution a continuance of the very humane and patriotic service which has characterized it in the past and

has so distinctly honored in a foreign land the zeal and scholarship of this country and in testimony thereof the University delegates as its representative at these ceremonies William Fletcher Russell, the Dean of its College of Education.

(Signed) W. A. JESSUP
President

(Seal)

[CANTON HOSPITAL]

TO THE PEKING UNION MEDICAL COLLEGE AND HOSPITAL GREETING: —

The Canton Hospital, the oldest in China, hereby extends its cordial congratulations upon this auspicious occasion, with earnest wishes for the fullest future success in the relief of multitudes, and the extension of the compassionate art of medical science.

(Signed) W. GRAHAM REYNOLDS
Chairman, Board of Directors

Canton, September 1, 1921.

To Dr. Henry S. Houghton, Ph.B., M.D., Director,
The Rockefeller Foundation, China Medical Board.

Introducing Dr. Chee Iu Ting, Alumnus,
Representative of the Canton Hospital.

[CABLEGRAM]

Washington, D. C.

To the PEKING UNION MEDICAL COLLEGE, PEKING.

Hearty congratulations at the formal opening of your hospital.

PHILIP SZE

[CABLEGRAM]

Washington, D. C.

To the PEKING UNION MEDICAL COLLEGE, PEKING.

I congratulate you upon completion new building, destined to be center medical training and research Far East. China at present suffers most from lack trained men lead nation safely through period transition. To this cause may attributed much of present unrest. It is gratifying note that Rockefeller Foundation recognizes China's

pressing need and undertakes give China's young men the best training. I take this opportunity offer Foundation best wishes for successful work in China.

ALFRED SZE

[CABLEGRAM]

London

To GREENE, ROCKFOUND, PEKING.

Hearty congratulations good wishes opening ceremony.

BALME
MOORSHEAD

[TELEGRAM]

Shanghai

To ROGER GREENE, ROCKFOUND, PEKING.

National Medical Association congratulate China Medical Board Rockefeller Foundation on completion of new Union Medical College Hospital buildings, and send greetings to all eminent scientists and others present at formal opening.

[TELEGRAM]

Dairen, Manchuria

To GREENE, MEDICAL, PEKING.

On occasion dedication building Union Medical College, I on behalf South Manchuria Railway Company take pleasure tendering you heartiest congratulation. It will stand out forever as one of grandest institutions in Far East for mitigating human suffering. No word suffices to express my profoundest appreciation and admiration of the spirit of Good Samaritan manifested in concrete form. Please convey my congratulation also to Mr. and Mrs. Rockefeller.

PRESIDENT HAYAKAWA
South Manchuria Railway Company

MESSIEURS:

L'Academie de Médecine de Paris, qui est la plus haute association médicale francaise, m'a chargé officiellement, de vous adresser

ses félicitations, il en est de même de l'Université de France. Je viens donc vous demander de me faire dire où et quand je pourrai m'acquitter de cette mission envers la Rockefeller Foundation et envers vous-mêmes.

Veuillez agréer, Monsieurs, l'expression des mes sentiments les plus distingués.

(Signed) TUFFIER

DEDICATION CEREMONIES

INVOCATION

By

The Rev. J. Leighton Stuart, D.D.

Creating and Controlling Spirit of the Universe, revealing itself in the beauty and wonder of this visible world, in the heart and conscience of man, and in that One who more than all others has disclosed Thy constant presence, Thy purpose for us, Thy pity for all in need of help and healing, and Thy power, we are gathered here this afternoon to dedicate this institution to the search for Thy truth which relieves human pain and removes human disease — an institution which, the buildings and the preparations now completed, begins its full activities. We invoke Thy blessing upon it. And because we believe that all the finer urgings of the human spirit, all the attainments of science and skill, are from Thee, therefore we thank Thee for all that these buildings, their equipment, their staff, their program, signify; for the ever-widening knowledge and understanding of those processes which make for human welfare; for the enlarging conception of brotherhood and of ministry to those in need; and for the gift making this possible, which has been so generous and notable in its conception. Because of the time and energy which have entered into all that concerns the great task it undertakes, therefore we ask Thy blessing upon it, upon all those who work here as they investigate and teach and plan all forms of enterprise and activity that make for health and happiness among the people of this nation, that they may extend knowledge and truth and hope, and that those who study here may go forth much benefited and enlightened, prepared for a larger usefulness; that they may catch the spirit of those who have made this possible — the spirit of service for others, of sacrifice for their fellows, of devotion to the highest ideals of the age, and of loving, devoted activity. Beginning with this day and through all its future career may it be guided and controlled by Thy spirit. We ask in the name of Him who more than all others has taught us that knowledge and power lie in concentrated effort for the welfare of our fellow-men. Amen.

PRESENTATION OF THE HOSPITAL AND MEDICAL SCHOOL ON BEHALF OF THE ROCKEFELLER FOUNDATION

By

George E. Vincent, Ph.D., President

The buildings which are formally opened today have been constructed and equipped by the Rockefeller Foundation through the China Medical Board. For the present they will remain the property of the Foundation, which puts them at the service of the Peking Union Medical College. On behalf of the Foundation I have the honor to welcome the Trustees and Staff of the College to laboratories, lecture-rooms, and hospital. Dr. Henry S. Houghton, the Director of the College, will now assume official control and preside over these opening exercises.

ACCEPTANCE ON BEHALF OF THE COLLEGE

By

Henry S. Houghton, M.D., Director

Mr. President:

On behalf of the College I gratefully accept the use of this great gift, with the humble hope that we may make it dynamic with intellectual and spiritual growth.

Honored Guests, Ladies, and Gentlemen:

It is my high privilege, on behalf of the College and its faculty, to welcome you to the ceremonies which mark its dedication to service. Many of you have come long distances to express by your presence here an interest in the work for which the College stands and to bear to us the felicitations of other institutions. We are deeply appreciative of this good-will and hopeful that it may prove a happy forecast of future helpful associations. I record with pleasure the greetings brought from many organizations in this and other lands by eminent delegates. The full list of these is in your hands.

In taking up the responsibilities and obligations which this new and beautiful setting opens to us, the faculty is not unmindful of the broad foundations laid by other hands, and of the devoted service given by those who first organized the Union Medical College. The ardor and unselfish enthusiasm of these men, some of whom laid down their lives in the line of duty, we may well emulate.

We realize also that the ceremony which dedicates these buildings is one in which the men and women to whom their use is committed should pledge themselves to the fulfilment of the purposes which the founders have had in mind. The primary function of this institution is to teach; to do so worthily implies high qualities not alone of professional training and experience but of scientific zeal and inspirational capacity. No motto for the teacher seems to be more apt than that suggested in the words of the Twenty-third Psalm, "My cup runneth over." The overflowing of impelling personality into the lives of others, the constant stimulus to intellectual acquisitiveness, comradeship in work — these are indices of success in a task

like this. A share in the promotion among our students of high ideals for service in the community and state, and of a thirst for righteousness, adds an obligation of which we are humbly sensible.

The program of the College includes, we hope, factors significant beyond the routine of teaching and research. In the enterprise are enlisted men and women of varied nationalities with a common interest in the educational problem. This fellowship of different nationalities in scientific fields may serve as a small example of international amity in the united effort for the peace and betterment of all peoples.

GREETINGS ON BEHALF OF THE PRESIDENT OF THE REPUBLIC OF CHINA

Presented By

HIS EXCELLENCY, W. W. YEN

On behalf of the President of the Republic of China and of the Chinese Government I have the honor to extend to you today very hearty congratulations and sincere wishes for the success and prosperity of the institution. It is perhaps only once in a lifetime that one has the privilege of attending the dedication ceremony of so important an institution as this, — an institution the full meaning and true worth of which is not to be measured merely by the magnificence of its buildings, by the wealth and perfection of its equipment, or by the number and quality of its professors and officers. Certainly at no other time in our history has a ceremony like this brought together from Europe, America, Japan, and every part of China, so large a number of distinguished visitors, celebrated scientists, eminent educators, and notable religious leaders. Peking, therefore, the capital of China, feels very much flattered and honored.

A distinguished fellow-countryman of mine recently made a tour of the world, and on his return was asked what had impressed him most during his visit to Europe and America. He replied without hesitation, "The application of science to every human activity." He is entirely right, for the greatness of modern Europe and America is due largely to the triumph of science. The employment of scientific methods in the intellectual and physical worlds has not only transformed and ameliorated every phase of human life in the Occident, but has also added breadth and brilliancy to its intellectual history. The progress made in medicine and surgery in particular is phenomenal, and, what is better, the discoveries are here utilized entirely and directly for the relief of physical pain and peril.

The world, and especially China, needs modern science, and yet not exactly of the kind that has devastated fertile and smiling valleys, that has maimed and killed millions of men in the bloom of

life, and has made widows and orphans in millions of homes, such as we have unfortunately witnessed during the late war. Rather we welcome in our land, where physical suffering is intense and universal, where ignorance of hygiene and sanitation leads to fearful mortality among the children, and shortens the duration of life among grown-up men and women, we welcome, I say, first and foremost, modern medicine and surgery, that branch of science which has for its motto the love of service, and which distinguishes itself above all others by its devotion to the teachings of the Great Healer.

Unaccustomed to scientific thought, China has been slow in adopting Western medicine and surgery, but I sincerely believe that with such a magnificent seat of medical learning established in the very precincts of our capital, the time will soon arrive when a truer understanding and better appreciation will dawn upon the masses, so that they will not hesitate to trust themselves entirely to scientific treatment.

In dwelling today on the magnificence of the present institution, let us also recall for a moment the memory of the men, who in their humble and modest but brave and noble way, laid the first foundations. The difficulties with which they had to contend in those days were such as would have discouraged and deterred men with less than apostolic faith and devotion. Nor should it be forgotten that the work was taken up and maintained with courage and steadfastness by a long line of missionaries and professional men, to whom we owe a debt difficult to repay, until the whole work is now taken over by the Rockefeller Foundation with a munificence that is surely unequalled.

The President has watched with interest and sympathy the growth and final completion of this Medical College and Hospital. He has charged me today on behalf of himself and of the Chinese Government to thank you, Mr. Rockefeller, your revered father, and the Trustees of the Foundation, for this great and splendid philanthropic act, an act that the present and future generations of China will ever regard with pride and affection. May the College and Hospital have all the success they deserve, and may they carry on their humane work of teaching and healing with ever-increasing magnitude and usefulness.

GREETINGS ON BEHALF OF THE MINISTRY OF THE INTERIOR

By

HIS EXCELLENCY, CHI YAO-SAN

I deem it a great honor to be able to be present at the formal opening of the Peking Union Medical College on September 19, in the tenth year of the Republic.

The promotion of education is the first step in the progress of the civilization of a nation, and the preservation of the people's health is an important function of philanthropic work. In the medieval age of China there were special functionaries who had charge of such duties, both in the Han dynasty and in the Sung dynasty. In the twentieth century, when much progress is being made in the material and spiritual worlds, the increase in the people's welfare depends upon the co-operation of the community.

The building of the Peking Union Medical College in China is of great benefit to the country, and the people of Peking entertain great hopes of its usefulness in the preservation of public health.

Upon the inauguration of your new work, which promises to produce many competent men, who will bring blessings to many, we feel very grateful for your enthusiasm and philanthropic spirit, which will strengthen the cordial friendship existing between China and America. I wish to exclaim with utmost sincerity:

Long live the Republics of China and of the United States of America!

Long live the Peking Union Medical College!

GREETINGS ON BEHALF OF THE MINISTRY OF THE INTERIOR

By

S. P. Chen, M.D.

Mr. President, Trustees of the Rockefeller Foundation, Faculty of the Peking Union Medical College, Ladies, and Gentlemen:

On this auspicious occasion it would not, I think, be inappropriate to say a few words on the progress of Western or modern medicine in this country, although it might seem to be a waste of your time to listen to any talk on this subject when we are actually gathered together to celebrate the opening of this institution which is a monument to the progress of modern medical science in China.

The birth of Western medicine might be taken as dating back to the time when lay missionaries, in the course of their work, found opportunities for the application of Western medical science. This was followed by the advent of the medical missionary and the establishment of dispensaries and hospitals. To carry on their work satisfactorily the medical missionaries were compelled to undertake the training of hospital assistants, and, as time went on, further development along these lines resulted in the founding of medical schools.

Modern medical schools in this country are innovations of this century; the earliest Chinese institution was one established in Tientsin, and the first foreign school was the one now replaced by the magnificent institution we are in. The new Peking Union Medical College is but an outward and visible sign of the progress of modern medicine in China. Other outward signs are seen in such actions of the authorities as the calling out of modern trained men to cope with serious epidemics of any kind, the increase in the number of medical institutions all over the country, the legalization of dissection, and so on.

There are, however, still other indications of progress known perhaps only to those who are in the profession. Personally, I cannot claim to speak from ripe experience, but ten years of practice in this

country would give one a fair idea of the nature of the changes taking place. I refer to the gradual change in attitude on the part of the general public towards modern medical science. Medical men who are connected with hospitals know that the number of people seeking treatment increases as time goes on. This, I admit, does not mean that the general Chinese public places such implicit confidence in modern medicine that the day of the quack is past — far from it — but when the question is viewed from all sides, it becomes evident that Western medicine is steadily gaining the upper hand. It is true that modern medicine is often appealed to as a last resort, sometimes even when no earthly help is possible. One comes across instances when the relatives, upon being asked the actual condition of the patient for whom they are seeking assistance, reply in a doubtful manner that the patient "hai yu i tien-rh ch'i" (is still breathing), or when they frankly admit that they have tried every other "fa tzu" (remedy); it is true that the greater number of cases for major surgery will still refuse operation, and that, on the whole, there still exists the dread of the knife. But, in spite of all these obstacles, modern medicine and surgery are slowly but surely replacing the older methods.

Progress for the next few years will necessarily be slow, and its rate will be materially influenced by the standard of medical education in this country. I was once informed by one of the officers of this institution that the policy of the Peking Union Medical College was to turn out quality, and not quantity, and that if it had only one student, that student was to be a sound one. If other teaching institutions in this country would view the education question from the same standpoint, I feel sure the onward march of modern medicine would be rapid. At present the large number of graduates turned out each year by certain of the medical schools serves only one purpose, and that is to bring discredit to modern medicine, and, in this way, to retard its progress. However, with the appearance of better manned and better equipped schools for teachers and the output of a higher grade product, the whole question will be automatically settled by the survival of the fittest. Official recognition of this fact would no doubt serve to advance the cause of modern medical science, and this recognition would best be shown by the placing of

medical education in general, and such questions as the licensing and control of medical practitioners in particular, under the independent care of a body of medical men of recognized standing. There will then be no need whatsoever to interfere with the old time physicians, as they must eventually die out. For, in the course of actual practice, there will be many opportunities, when the quack has got to the end of his tether, for asserting the superiority of modern medical science over the more antiquated methods; and, with an increasing number of properly trained men who are reasonably sure of their ground, such opportunities can be taken advantage of, and the more they are encountered the quicker will be the progress of modern medicine.

We look to such institutions as the one whose inauguration we are here to celebrate to produce such men, and, in this way, to assist in advancing the cause of modern medical science in this country. I am therefore happy and proud to be able to have this opportunity of wishing the Peking Union Medical College every success in its great work.

GREETINGS ON BEHALF OF THE MINISTRY OF EDUCATION

By

His Excellency, Ma Lin-yi

I am glad to see the progress which has been made by the Union Medical College in Peking. In recognition of those who have helped to make this college such a large and prosperous institution, I must express my sincere thanks to the Rockefeller Foundation and to the American educators and scientists who are working here. And because today is the day for celebrating the completion of the new buildings, it is a great pleasure for me to be present.

In regard to medical science: It is needless to say that much progress has been made in Western nations, and that when it was introduced into China it caused great surprise because of its new methods of treatment. In my opinion there was in olden times no difference between the medical theories and practices of the East and the West, for in those days there were similar methods of determining the cause of a disease and attempting to find a cure for it. But later Chinese medical study became more philosophical, while Western medicine followed the progress of modern science. Thus the systems have come to differ, and, although Chinese medical study has a long history and a profound philosophy, we deem it indispensable to adopt the scientific spirit and the scientific method of Western medical education. We hope that this college, using both Chinese philosophy and Western science may be able to discover new theories and make great contributions to medical history.

Because I am acting as Minister of Education and because I take a great interest in the promotion of medical science, I will give my hearty support to this college, and I hope it will not only render good service to China, but also make valuable contributions to the world.

RESPONSE FOR THE CHINA MEDICAL BOARD

By

ROGER S. GREENE

Mr. Chairman, Your Excellencies, Ladies, and Gentlemen:

It is my special privilege on behalf of the China Medical Board of the Rockefeller Foundation to thank the representatives of the Chinese Government for their kind greetings and for their good wishes for the success of our enterprise. We shall do our best to merit the confidence that they have expressed.

It is not my part, in the presence of so many distinguished scientists, to discuss the educational policies which should govern this youthful institution. I should like, however, to take this opportunity to speak of some of the hopes which I cherish for the future of this school as one of many agencies tending to promote better understanding between nations.

The Peking Union Medical College happily seems to possess in its organization and location not a few advantages which should help to qualify it to play such a part. Beginning as a united effort of British and American missionary societies, its international character has fortunately been preserved in the new organization of its board of control. In the faculty and administrative staff, its international quality is still more marked. Besides Americans, British, and Canadians, and some from the continent of Europe, we have the participation of a large and growing number of Chinese in all branches of the work, and, as time goes on, within the limits imposed by the necessity of using a single language as the teaching medium, I hope that representatives from other nations may join our forces. With the supply of good medical teachers lagging so far behind the demand, the advantage of being able to ignore national lines in the selection of the staff are obvious, and the possibilities of intellectual stimulus from the mingling of men with different types of training are great.

But the point on which I should like to dwell for a moment is the value of the international character of the organization as another

demonstration of the possibilities of co-operation between nations when all are working for common and practical ends, so important, so absorbing, that they overshadow petty national differences. We had such a demonstration in the great war. Here in China we have lately seen in the concerted efforts made to relieve the famine, an example of how men of different nations have been able to work together in an effective and friendly way. Let us remember the important work of such an inconspicuous organization as the International Postal Union. We have lately attempted a union of national Red Cross societies, and the moment seems almost ripe for an international health service that shall collect and disseminate information, and be prepared to offer its assistance in times of emergency to those nations who are members. Men accustomed, as the staff of this College will be, to co-operating with people of other nationalities in countries other than their own, should be specially qualified for such international service and should therefore help to furnish one of the elements necessary for its success. International co-operation in political affairs seems to be attended by endless difficulties, but as we acquire a better understanding of one another by working together in international trade, in communications, education, scientific research, public health, and other normal human activities, the final step to some form of political organization that shall safeguard the peace of the world may prove less difficult and less revolutionary than it has hitherto appeared.

We hope that this school may help in particular to create a better understanding between China and the countries of the West which we represent. It comes not only to give but also to receive, for probably many of its teachers would not be here unless they hoped to learn perhaps more than they can expect to teach; and this is well, for the more success they have in preserving the attitude of the student in their own work, the better will they succeed as teachers. This school is so situated that its workers may not only hope to learn much from their studies in China, but they may also profit by closer association with the important Japanese scientific institutions than is feasible for our scientists at home. The proper development of such relations may do much to lessen in this school the feeling of isolation which so often depresses scientific workers in a new field.

While we hope that our efforts will result in bettering the condition of the Chinese people, it is certain that if we succeed in attaining that object, we ourselves and all other nations having dealings with this great country will likewise benefit; for modern transportation has so intertwined the interests of all parts of the world that each nation is bound to gain eventually in some degree from the increased strength and prosperity of the others.

I fear that these remarks savor of the platitudes common on such occasions as this, and often uttered even by those who are doubtful of the truth of what they assert. Unless my proposition is correct, however, as I am confident that it is, I see little hope for the permanent maintenance of friendly relations between East and West. Here we have two great groups of peoples, on opposite sides of the Pacific, one group living in comparative prosperity and the other in relative poverty. Whatever may be the moral and spiritual compensations that accompany this material poverty, and some of them are not to be ignored, the fact remains that human beings all over the world do strive for security against hunger and cold and for material wealth for themselves and their families. The contrast at present between East and West in this respect is too great to be a permanent condition. Either those who have little or nothing must be enabled to improve their condition at home, or they will eventually go to the country of those who have, and in such numbers as to cause a violent upheaval in the country which they invade. At present there seems to be nothing to prevent such an invasion from ultimately taking place, except armed force or the removal of the incentive to such mass movements of people from one country to another. In the case of China this incentive can probably be removed only if we help her to become as strong and prosperous as we ourselves are. Therefore those Westerners who are working for the development of China, whether in industry, transportation, education, or public health may be assured that if they succeed in promoting the prosperity and happiness of the Chinese people, they will at the same time render an inestimable service to their own countries.

While sudden mass movements of people from one country to another are perhaps justly dreaded, it is to be expected, and it is probably desirable that there should be an increase in the move-

ment of individuals and their families from one country to another in pursuit of those occupations which naturally take men abroad, of which perhaps the most important is a mutually advantageous commerce in ideas, for there is no doubt that each side has much to learn from the other. Some of these individuals and families who migrate will remain permanently in the foreign country which they visit. The people of America, and to some extent the people of Europe, have not been sure as to what should be their attitude towards such alien elements in their population, even when the difference in race has been slight. Where the difference has been great, as in the case of Japanese and Chinese in the United States, the combination of racial prejudice and not unreasonable fear of serious economic consequences, has led not only to the apparently necessary measures for the economic protection of American labor but also to attempts at other kinds of discrimination which seem to many Americans both unnecessary and unjust. This inhospitable attitude is defended partly on economic and partly on social or biological grounds. If it is rightly taken, it may be possible to justify it by arguments based on economic and biological facts, ascertained by scientific investigation, or it may be possible to prove by the same methods that the fears which have led to discriminatory measures are unfounded. But the vital facts, certainly in the biological field, are still to be discovered. Whatever the results of scientific study of the emigration question by anthropologists may be, and even if, as seems possible, no final answer can soon be given, the fact that the question has been referred for dispassionate investigation to experts will put the discussion on a higher and calmer plane, and will lessen the danger of hasty action induced by prejudice. If the answer is found we shall have a basis for a permanent settlement, permanent because it will be regarded by all reasonable persons as just and necessary. If the workers in the anatomical and physiological laboratories of the Peking Union Medical College can throw some light on this one question the effort and expense involved in the establishment of this school will be many times repaid.

This world is now discussing disarmament, with eager longing for relief, both from the burden of large armies and navies and from the fear of wars which such armament tends to precipitate, but with

grave doubt as to the practicability of the proposal. If we are to make real progress towards our ideals of peace between the nations, must we not divert to the positive task of creating conditions favorable to peace, at least part of the enormous energies and resources which are now devoted to the negative work of military defense? One hesitates to place limits on the benefits which might result if but a tenth of the time and money given to our military and naval establishments were applied to investigation of problems threatening the peace of the world, to enterprises tending to foster the co-operative spirit, and to the proper education of public opinion. Let us hope that the Peking Union Medical College may play at least a humble part in such a campaign of peace.

RESPONSE FOR THE ROCKEFELLER FOUNDATION

By

JOHN D. ROCKEFELLER, JR.

Oliver Wendell Holmes says in his *Autocrat of the Breakfast Table* that every individual is a combination of three persons: first, what he thinks he is; second, what his friends think he is; third, what he really is.

I am here today representing not three, but four personalities. First of all, I have come to China representing my father, who established the Rockefeller Foundation. I am here, secondly, as a representative of the Foundation itself, not inappropriately called my father's child. Thirdly, I represent the China Medical Board, the child of the Foundation, hence the grandchild of my father. And lastly, I am here as a Trustee of the reorganized Peking Union Medical College, the adopted child of the China Medical Board, hence my father's great grandchild. It is fortunate for this assembly that I am not particularly interested in genealogy, for otherwise I might insist on your climbing with me through the numerous branches of this family tree.

Speaking first for my father, and as his representative, may I say how much I wish he were with us that he might himself see and rejoice in what is here being accomplished, and that you might feel the inspiration of his simplicity and greatness of character. But since that cannot be, I am happy to be able to read you a cable message which has just been received from him: "My highest hopes are centered on the Peking Union Medical College which is about to open its doors. May all who enter, whether Faculty or Students, be fired with the spirit of service and of sacrifice and may the Institution become an ever-widening influence for the promotion of the physical, mental, and spiritual well-being of the Chinese Nation."

On behalf of the China Medical Board, Mr. Greene, the Resident Director, has already spoken. Therefore, in the few moments at my disposal, as a representative of the Rockefeller Foundation, the grandparent of the baby, — an adult infant to be sure, — whose re-

christening we are here today to celebrate, I shall devote myself chiefly to the youngest offspring of this family tree, the Peking Union Medical College, of whose origin, prenatal history, birth, and early development I desire to speak briefly.

As my father's interest in human betterment widened, and it came within his power to render service to his fellow-men beyond the boundaries of his own country, his attention was naturally directed to the great Chinese Nation, with its history running back thousands of years; its early achievements in industry; its literature and art, so rich and beautiful; and its population, greater than that of any other nation on earth. Feeling that perhaps by seeking to assist in the establishment of high educational standards the greatest service could be rendered to the Chinese people, my father made possible the sending of a commission from the University of Chicago, in the year 1909, to study the educational conditions of China. The commission, composed of Dr. Ernest D. Burton, Professor of Theology, and Dr. Thomas C. Chamberlin, Professor of Geology, after thorough study, recommended the establishment at Peking of an educational institution for the teaching of the natural sciences. However, so gigantic seemed the undertaking and so important the avoidance of a false step, that further study and conference were deemed desirable before any move was made. This led to the conclusion that to focus thought and effort on one group of sciences, namely the medical sciences and their application, was the wiser course to follow. A second commission was therefore sent to China in 1914, consisting of Dr. Harry Pratt Judson, President of the University of Chicago, Dr. Francis W. Peabody, of the Medical Faculty of Harvard University, and Mr. Roger S. Greene, at that time Consul General of the United States at Hankow, now Resident Director in China of the China Medical Board. This group was requested to study the medical needs of China and the opportunities for co-operation in meeting them. The commission returned convinced of the wisdom of the conclusion already reached and recommending the establishment of a medical school and hospital at Peking and a similar medical center in Shanghai. Before final action was taken, however, a third commission went out in 1915, composed of Dr. William H. Welch, of the Johns Hopkins University Medical School, Dr. Simon

Flexner, of The Rockefeller Institute for Medical Research, Dr. Wallace Buttrick, Secretary of the General Education Board, and Dr. Fred Gates, also of The Rockefeller Institute. The report of this commission corroborated the findings of its predecessor and cordially endorsed the program of establishing the two medical centers previously recommended. Going further, it advised entering into an alliance with the Peking Union Medical College, which had been in operation for several years, and building upon that foundation the medical school proposed for Peking.

Let me pause just here to say that in the light of subsequent events and experience it became clear that the main objects sought could be attained by the development of a medical school in Peking alone.

In the meantime, the Rockefeller Foundation had established the China Medical Board as a subsidiary organization to deal with medical and health questions in China. The China Medical Board therefore entered into a contract for the purchase of the land and buildings of the Peking Union Medical College and the reorganization of its Board of Trustees. The new Board was to consist of thirteen members, each of the organizations which had been associated in the founding and development of the College to have one representative, namely: the Medical Missionary Association of London, the Society for the Propagation of the Gospel, the London Missionary Society, the Board of Foreign Missions of the Presbyterian Church in the United States of America, the Board of Foreign Missions of the Methodist Episcopal Church, the American Board of Commissioners for Foreign Missions; the seven remaining Trustees to represent the China Medical Board. The contract also contained an agreement on the part of the China Medical Board to erect the necessary additional buildings and provide such maintenance funds as in the judgment of the Board might be required until the College should become permanently established and its future should be assured.

The purpose of the China Medical Board in entering into this contract was to develop in China a medical school and hospital of a standard comparable with that of the leading institutions known to Western civilization. In this contract it was proposed to offer to the Chinese people facilities for acquiring a thorough knowledge of and training in Western scientific medicine. While it was intended that

the college should lay emphasis upon the training of promising men and women for positions as teachers and investigators, it was of course realized that many of its graduates would enter the service of the community as well-equipped physicians and surgeons. It was also a part of the plan to provide short courses for medical missionaries and Chinese doctors throughout the Chinese Republic that they might be enabled to keep pace with the rapid strides made by modern medicine and might be helped to make of the greatest service the many useful medical enterprises which they were carrying on. But above all it was hoped that this new medical center might so commend itself to the Chinese people that it would stimulate them to develop similar institutions in various parts of China. For the China Medical Board recognized from the outset that only the Chinese Nation itself could cope with a task so colossal as the establishment of modern scientific medical education throughout the Republic and that all Western civilization could do would be to point the way.

There have been purchased for the Peking Union Medical College considerable areas of land and fourteen main buildings. Fifty-five residences and auxiliary structures have been built or remodelled, all of which are now complete and ready for occupancy. The College is now offering to both men and women students the regular medical courses with its practice work in dispensary and hospital, and a pre-medical course as well. It is also conducting a training school for nurses.

As regards graduate instruction, it is intended that in certain subjects, where the need is great, short courses such as are now being given to medical missionaries and Chinese practitioners will be provided. It is believed, however, that a more valuable service will be rendered by affording opportunities for more prolonged and thorough training of those suitably qualified by receiving them, in necessarily limited numbers, for a period of months or even a year as volunteer assistants or special workers in the various departments, whereby they become for the time being a part of the organization.

While the primary function of the College, as of every medical school, is educational, opportunities have been provided in its laboratories and in the Hospital for the prosecution of research in the

fundamental medical sciences and clinical subjects. A medical school imbued with the scientific spirit and prepared not only to impart but also to advance knowledge is capable of rendering an inestimable service to China in the influence which it may exert upon the standards and the methods of medical education, in the training of teachers and leaders in the profession and in contributing to the solution of the many problems of disease in this country. Abundant experience has demonstrated that teachers gifted with the inclination and capacity for productive investigation are able to combine with their duties as teachers the prosecution and the stimulation of research and to gather about them advanced students and special workers whose contributions extend the reputation of teacher, department, and school.

A grateful service which the College will be glad incidentally to render to the community through the Hospital and Dispensary, is the alleviation of suffering. But the number thus reached will of necessity be relatively small, for it must be borne in mind that the Hospital is primarily a teaching institution, which while affording the best care for patients, exists, first of all, for instruction and research. Moreover, while the College has not been established to serve the foreign community it will do all that is possible, within the limits of its primary purpose, to receive serious cases into the hospital, to assist private physicians in diagnosis, and to enter into consultations. Obviously, however, the medical staff cannot, in justice to its first duty of teaching and research, be expected, except in rare and critical cases, to make calls upon patients in Peking or to undertake journeys to distant points. But we are happy in the belief that other hospital facilities now available in Peking and an increasing number of well-trained medical men will be able to give adequate care to foreign as well as to Chinese patients.

Toward the realization of the purpose which has animated it from the outset, the China Medical Board has spent in developing the Peking Union Medical College well nigh twice the sum which the present physical plant and equipment would have cost before the war. Several factors combined to bring about this result. Just as the building program was well under way, the rate of exchange doubled, an item alone which increased the cost of the plant by

nearly two millions of dollars gold. Moreover, as a result of the war, freight rates rose so rapidly and the delays in shipping were so great that very considerable extra cost was thereby involved. Then, too, the fact that the China Medical Board had had no previous experience in building in the Orient doubtless somewhat increased the total outlay. Probably a fair valuation of the physical properties of the College today, including the land, would approach five millions of dollars gold.

In drawing plans for the medical buildings and hospital, it has been necessary to follow Western design and arrangement in the interior of the buildings in order to meet the requirements of modern scientific medical practice. At the same time we have deliberately sought in so far as possible, although at no little additional cost, to combine with utility of interior the beauty in line and decoration of the Chinese exterior, particularly as regards height, roof structure, and ornamentation.

This we have done in order that the Chinese people for whose use these buildings have been constructed may feel at home in them and be drawn into closest sympathy and co-operation with the work which they house, and also as a sincere expression of our appreciation of the best in Chinese architecture. That we have been successful to some degree in stirring the interest and appreciation of the Chinese is evidenced by the following excerpt from an article by Sam Dean entitled, "Singing Craftsmen of Peking," which appeared in the August (1921) issue of *Asia.*

"Master Chinese craftsmen have told me, in expressing their opinion of the Rockefeller Hospital at Peking, that no other building erected in China in the past century was so profound an inspiration to Chinese artisans. They did not like the window-casings, they felt the lack of the massive, deep-shadowed effect that columns would have produced and they thought the unsupported walls too frail for the roof, but, because the building was one in which the soul of a people could express itself, they traveled long distances for the privilege of working on it, even in the humblest capacity. Men who were master stone-carvers in their own districts were willing to work as coolies, if only they might say they had been employed in the construction of this building. Farmers from the Western Hills,

descendants of the architects that built the Peking palaces, were content to haul dirt on wheelbarrows if they too might have some share in this masterpiece. I once met an old artist, a painter of temples from his boyhood, who had painted certain of the figures near the roof of the hospital. From the ground they were barely visible, but he had put the training of a lifetime and all his soul into the work. 'It is,' he said, 'my monument.'"

Surely it is not too much to hope that the same fidelity and devotion to their task which characterized some of the artisans who erected those buildings, may be inspired by the buildings in the students who use them.

But we have realized that stone and wood, however cunningly and skilfully fashioned, and equipment however complete, cannot make a medical school; that this result is dependent upon the quality of mind and heart which the faculty brings to bear in its work. Hence the United States, Great Britain, Canada, as well as China, have been drawn upon in making up our family, which is composed of men pre-eminently fitted for their work and entering into it in a fine spirit of loyalty and enthusiasm.

Particularly gratifying is it to be able to bear testimony to the excellent work and promising character of a number of the young Chinese members of the staff, whose development we are following with the greatest satisfaction.

We have realized, too, that although we might give to the Chinese medical students who pass through the College training as good as is to be had anywhere, that alone would fall far short of equipping them for their life work as the highest type of medical practitioner should be equipped. For only as their professional skill goes hand in hand with high character, only as they are inspired with the spirit of service and of sacrifice referred to in the message from my father, will our graduates be of the most value to their fellow-men and to their country. And it is because we believe that the highest character is built upon the deepest spiritual foundations alone that we have sought to bring together a medical faculty not only with the best scientific equipment but possessed at the same time of the finest idealism. In other words, it is the desire of the Peking Union Medical College to offer to the people of China the best that is known to

Western civilization not only in medical science but in mental development and spiritual culture. While, therefore, we shall willingly minister to the bodily needs of those who come within our doors seeking physical aid only; while we shall gladly afford training for the minds of those who come for that purpose, and while it is our profound conviction that the best in any man can be realized only as his nature becomes receptive to the highest spiritual influences, at the same time it is not our purpose to force upon any one that which he does not wish; nor shall we refrain from serving those who come to us for aid along any one of these three lines of human betterment because he does not wish help along all three.

With the Medical Missionary Boards which have been most zealous in the development of medical missions, and with the work which they have undertaken, the Peking Union Medical College wishes at all times to be in most cordial co-operation. We are here to supplement, not to supplant, what they are doing; to aid, not to impede, them in their efforts. In fullest sympathy with the missionary spirit and purpose, we are desirous of furthering it as completely as may be consistent with the maintenance of the highest scientific standards in the Medical School and the best service in the Hospital. We would ever show respect for the genuine spiritual aspirations, evidenced in service and sacrifice, of those who come within our doors, whatever their views, — for after all is it not a fact that the final test of true religion is the translation of that religion into the highest type of life?

Rome was not built in a day, nor can the ideals which animated the founders of the new Peking Union Medical College be realized in a day, or a year, or a decade. A mushroom growth is short lived. The most stable and enduring structure is that which is built on deep and broad foundations. This enterprise was entered upon, as has already been pointed out, only after years of careful study and deliberation. The purpose of those who are back of it has never weakened or changed. The one danger to be carefully avoided is the temptation to too rapid growth and a superficial development. Gradual growth alone gives assurance of stability and permanence. A frank recognition of this danger at the outset and concerted action on the part of the trustees and faculty in standing resolutely

against it will insure its avoidance. Patience will be needed on the part of the faculty, the students, and the public in the development of this institution. Certain departments may not be fully organized or completely equipped for some time to come and a few may not even be started until later. We shall endeavor, however, to maintain a high standard for those departments which have been established. So long, therefore, as all those related to the enterprise are working together in a spirit of sympathetic co-operation toward the attainment of the ultimate ideals which we have set before us from the outset, each step taken will be a step of real progress in reaching the final goal.

In order that one of the foremost objects of the China Medical Board in building up the Peking Union Medical College may be attained, namely, that the College may serve to stimulate the development by the Chinese people of similar institutions, it is essential that the current cost of operating should always be kept on a conservative level. If a policy other than this is followed and a school set up here more expensive to maintain than comparable institutions in America and Europe, not only will a disservice have been rendered to the cause of medical education and hospital development throughout the world, but the Chinese people will not be so ready to undertake the creation and maintenance of similar institutions in other parts of the Chinese Republic.

Clearly, whatever Western medical science may have to offer China, it will be of little avail to the Chinese people until it is taken over by them and becomes a part of the national life. So we must look forward to the day when most, if not all, of the positions on the Faculty of the Peking Union Medical College will be held by Chinese; when the Board of Trustees, while embracing appointees of those bodies which founded the institution, as well as other representatives of Western civilization in China, will include leading Chinese; and when such current support as the institution may need beyond that derived from tuition fees and such endowment as may be set aside by its founders, shall be derived from Chinese gifts and governmental subsidies, as is the case with medical institutions of similar rank in other countries of the world. Let us then go forward with one accord towards the attainment of this objective which will make

permanent the establishment on Chinese soil of the best in scientific medicine that the world can offer.

Recently, when the pneumonic plague appeared in Shansi, the Minister of the Interior assigned certain physicians, among them Dr. Yu Shu Fen, to combat it. Dr. Yu succumbed to the disease, and realizing that he could not recover, dictated a farewell message in which this remarkable paragraph occurs: "With my enthusiasm for plague prevention I overstepped the bounds of convention and in my constant contact with the plague accidentally contracted the disease. I am dying for the people. I have no complaint." Just a few days before his death Dr. Yu had written in the guest book of Dr. F. F. Tucker of Tehchow: "I come to fight the plague and to put into practice God's love for men."

When the Peking Union Medical College faculty is manned with Chinese professors of Dr. Yu's type, bringing to bear upon the students of the College the influence of such lives, and when men of that caliber are each year being graduated from the college to spread abroad throughout this great land the healing of the body and the inspiration of the soul of the Chinese people, the spirit of service and of sacrifice, in which this institution was conceived, will have been immortalized and one of the chief purposes for which the college was founded will have been realized.

ADDRESS AT THE RECEPTION AT THE PRESIDENT'S PALACE

By

HIS EXCELLENCY, PRESIDENT HSÜ SHIH-CH'ANG

China and America are far apart, but cordial relations are maintained between us, because both have adopted the same form of government and both are striving for universal peace. Americans are keenly interested in public welfare and the Chinese also are a charitably disposed people. The aims of the two Republics converge and their friendship daily grows more intimate.

It gives me special gratification to have this opportunity of receiving this large and distinguished gathering from different parts of the world to celebrate the opening ceremonies of the Peking Union Medical College. It is indeed a brilliant assembly. One of our philosophers, writing on Universal Love and Altruism, said that a physician is the Minister of Love and Humanity; his virtue dispenses benevolence, his knowledge brings healing.

The Peking Union Medical College has been established for many years and hundreds of students have been trained. Its hospital has treated all kinds of diseases and treated many patients with marked success.

The new buildings are solid structures, exquisitely finished, combining the best features of Chinese and Western architecture and equipped with the most modern appliances. Their completion surpasses all past efforts of a similar nature in China. They exemplify the principle of Universal Love and Altruism. They will greatly benefit our society and arouse in the hearts of our people a broader love, a deeper sympathy, and a higher effort to imitate the noble example set before them. Our philosopher's words will then be fulfilled and I shall not be alone in feeling gratitude for the benefits to be derived therefrom. I take this opportunity to thank you, Ladies and Gentlemen, for your presence and I wish you every success and prosperity.

EVENING ADDRESSES

MEDICAL EDUCATION IN CHINA: A SURVEY AND FORECAST

By

EDWARD H. HUME, M.D.

EARLY HISTORY

In the year 1692 the Emperor K'ang Hsi was seized with a fever that threatened his life. The court physician employed every means known to Chinese medicine but failed to cure him. Then the Emperor recalled that the Jesuit Fathers, Gerbillon, Bouvet, and de Fontenay, had boasted of the virtue of a drug recently brought from Europe, quinine, to which the Emperor had himself given the name "divine remedy." Failing to be cured by the court doctors, K'ang Hsi asked that he be given the European remedy, but the official physicians refused to permit this because they considered it too rash to experiment with an unknown remedy on an imperial personage. Three of the physicians urged that all treatment be deferred until the nature of the disease should be more fully investigated. The Emperor, however, disregarding their advice took the European remedy and on the evening of the same day was without fever. Although there were slight recurrences during the days that followed, the Emperor again insisted on more thorough treatment with the Peruvian bark and soon was entirely well.

Gathered as we are tonight in this capital where the record of imperial days is writ large on every hand, — and coming together as the guests of this institution where East and West have so truly met, the West coming as a student to the East to be taught in the ways of architecture, while bringing to it some knowledge of the common problems and needs of mankind's well-being, so that both may join hands as they seek to understand and solve them — we do well to inquire of the imperial patient. It is easy to imagine him, resting beside one of those enchanting lakes just over yonder, bringing to mind as his convalescence progresses the story of what China has done for medical education. The open lotus blossoms seem to reach

up from the water and beckon him back to the early days. Had not Shen Nung, the Father of Medicine, tasted a hundred herbs? Was it possible that he had found anything so bitter as this foreign bark? And had not Huang Ti, who followed him, in collaboration with his chosen prime minister Ch'i Pei, compiled the *Classic of Internal Medicine* and other books that were to be the means of instruction for untold hundreds of years?

The Emperor turned rapidly from volume to volume, not stopping to read again the story of Ho and Huan, the great teachers before the time of Christ; or to recall other medical names that had become glorious in history. In the Sui dynasty (581 to 618 A.D.) he found that medicine had already become departmentalized, that special chairs were established, and that pupils were enrolled in each. It was during this dynasty that Fuyiwaiyi, a Japanese student of medicine, probably the first of those from his nation, came and studied in China for fifteen years. Not until he came to the records of the Sung dynasty, however, did K'ang Hsi find evidence of true medical schools.

It was while William the Norman was putting in order the Island Kingdom where only two years before he had been victorious, that Shen Tsung called together the scholars and organized the medical teachings of the early masters, giving continuous instruction, and arranging for regular examinations. Still later, when the Mongols were at the height of their power in China, one of the officers from the Great Court of Medicine was entrusted with the teaching of selected students and with the responsibility of determining by periodical examinations their fitness for public use. Grateful that his country had been active from the earliest days, the Emperor gave the books back to the attendant and rested once more.

We, too, must give our measure of honor to these masters of the early days, who carried in their hearts the sufferings of their countrymen and strove to find and supply remedies for their healing. And yet (I quote from Dr. Wu Lien Teh), "in spite of some excellent methods of treatment and a long list of useful drugs handed down by the ancient teachers of medicine, nothing has been done by their successors either to improve knowledge or keep abreast of the times. The results are deplorable, and the majority of native-trained

physicians of today are completely ignorant of the true causes of most diseases, their methods of diagnosis, and their modes of prevention." "Instead of dissection," says a teacher writing in the Soochow Alumni Medical Journal, "superstitions have prevented our examining the body. Our medical teaching is founded on empty theory. Instead of picturing the heart as the centre of the circulatory system, we call it 'the prince.' The liver, instead of being described in its relation to metabolism, is said to be 'the commander-in-chief.'" Is it any wonder, then, that even as early as the Chou dynasty, a thousand years before Christ, officials who knew the inadequacy of medical knowledge, warned the public against swallowing the medicine of any physician whose family had not been in practice for at least three generations? Or that a decree went forth requiring that all medicine administered to a ruler of the state must first be tasted by the prime minister? Surely it must have proved difficult for the Jesuit priests who provided the quinine for K'ang Hsi to find favor with his Chief Executive!

MODERN MEDICAL EDUCATION

An old Rugby schoolboy, Thomas Richardson Colledge, founded the first dispensaries in China; first in Macao in 1827 and the following year in the city of Canton. Joined in 1834 by Peter Parker, a Yale graduate, recognized as the first medical missionary in China, he soon found that they must train up assistants, and also go to the public for support for their medical undertaking. Thus there came into being the Canton Medical Missionary Society, the first of its kind. This Society was formed to encourage Western medicine among the Chinese by affording an opportunity for Christian philanthropy and service; and to cultivate confidence and friendship, thus introducing the Gospel of Christ in place of heathenism. But much more than this, it was "to provoke inquiry into truth by opposing exact science to superstitious ignorance (It must be remembered that when they spoke of exact science no single one of the pathogenic bacteria had yet been discovered.); to educate Chinese youths in Western medicine; to advance general medical knowledge by the reflex benefits which will accrue from scientific discoveries in China." I doubt whether the Trustees of the Peking Union Medical College, even

with the full program of the Canton Society before them, could draw up a statement that would more adequately express the objects of this institution in which we are assembled.

It was thus under Parker and Colledge, as early as 1840, and later under Kerr of the same hospital, that modern medical teaching began. In 1870, medical students were formally admitted and the translation of textbooks was taken up in earnest. In 1879, the first Chinese women to begin medical studies entered this school. In the meantime, however, Benjamin Hobson of the London Missionary Society, while practising in Hongkong, in Canton, and later in Shanghai, lectured, taught, and translated continuously.

Forty years ago the Viceroy, Li Hung Chang, grateful to Dr. Mackenzie for saving the life of Lady Li, provided quarters in Tientsin for the opening of medical school work; gave Dr. Mackenzie the funds with which to carry on his classes; imposed no hindrance to religious teaching; and thus started the earliest school of medicine among those that are still active. During Mackenzie's lifetime nineteen men graduated; but they did not get posts commensurate with their training. The school, however, is still in existence and is now the Navy Medical College.

Still another formal experiment was made by Dr. W. W. Myers at the David Manson Memorial Hospital in Takow, Formosa. Three students were graduated in 1888 but they, too, were unable to get suitable posts in this country and settled in the Straits Settlements. From those days until now men of vision have given personal instruction or taken part in the founding of schools. From North to South we shall find the evidences of their devotion. They won confidence for Western medicine and exerted a deep spiritual influence and, more than that, they sent out pioneers who through daily association with the Chinese, gave them inspiration for service. I wish we might count tonight those in this hall who have had valiant aid from men thus trained. And that we might pause to give personal thanks to the leaders at schools like those at Hankow, Nanking, and Soochow, who, after instilling a love for medical missionary service into the hearts of men, saw the wisdom of uniting their forces with those of other centers. It is nearly a hundred years since Colledge started his first dispensary and forty years since Macken-

zie launched the first modern medical school in China! What is the record of their successors today?

An inquiry made in August, 1921, showed that there were twenty-four medical colleges in China. Eleven of these are Chinese institutions, eleven are under foreign control, and two others are managed co-operatively by Chinese and Westerners. Of the Chinese colleges, three are supported by as many ministries of the Central Government (the Board of Education College, the Army Medical College in Peking, and the Navy Medical College in Tientsin); four by Provincial Governments (one at Paoting in Chihli, one at Hangchow in Chekiang, and two in Kiangsu, the Central Provincial College at Soochow, and the former German College now located at Woosung); and four by private groups, the Nantungchow College and the Dung Dai College in Kiangsu; a woman's college at Hangchow in Chekiang; and the Kwong Wah College at Canton.

Of the foreign-controlled colleges, two receive a measure of government aid (the Japanese South Manchurian College in Mukden and the Hongkong University Medical School under British control). This one in Peking, whose guests we are, is under a board of thirteen trustees, six representing the six missionary societies originally maintaining the Union Medical College and seven representing the China Medical Board of the Rockefeller Foundation. The remaining eight colleges are conducted by missionary societies. Three of the eight are union institutions in which British and Americans co-operate (Tsinan, Foochow, Chengtu); British and Danish teachers co-operate at Mukden in another; the Peking Women's Union College is an American institution; the British China Missionary Society maintains a college in Hangchow, while the other two are conducted by American societies — St. John's in Shanghai under the Episcopal Board, aided by contributions from the University of Pennsylvania, and Hackett Medical College at Canton. The other two colleges are the Hunan-Yale College of Medicine, conducted co-operatively by the faculty of Yale-in-China at Changsha and a society of Hunanese leaders interested in medical education; and the Kung Yee College in Canton, controlled by a Chinese board, but under the professional supervision of American teachers.

A few facts about these colleges should be considered. As regards

their location: twenty-two are in provinces bordering on the sea (three in Chekiang, six in Chihli, one in Fukien, five in Kiangsu, four in Kwangtung, two in Manchuria, one in Shantung); while the other two are in Hunan and Szechuan, respectively, far in the interior. Grouped according to the language used as the medium of instruction: fifteen teach in Chinese, five in English, and one in Japanese; while two use both Chinese and German, and one Chinese and French. Fifteen of the colleges are at present teaching only men; three are exclusively for women; while the remaining six admit both men and women students, though in two of the six, women are as yet registered only in pre-medical classes.

It is impossible at the moment to give exact figures as to the total number of graduates from these twenty-four colleges. There are certainly not over 3,000. Add to this those who were taught privately or in colleges that have ceased to function, and we shall get a grand total of probably not more than 4,000 or 4,500 as the figure representing those who have received a more or less full measure of personal or institutional training in Western medicine. The proportion of these that has had sufficiently thorough preparation and that has developed sufficiently sustained ideals to justify the designation "fully qualified" is exceedingly low.

The total number of medical students in China in regular colleges is a little over 2,000; of which number only ninety-five are women. In addition to this number, the six colleges that require thorough pre-medical science courses have between one and two hundred students under their immediate supervision.

The numerical strength of the faculties at the different colleges varies from four at Foochow to forty-three at the Peking Union Medical College. (It is only fair to state that since this report was commenced the Foochow College has decided, on account of the shortage of teachers and other factors, not to continue instruction for the present.) These numbers are in addition to the faculties of the pre-medical schools.

The variations found in the reports on budgets are extreme. The Hangchow Woman's College reports a total budget of $2,500 silver; while the total budget of the Peking Union Medical College was $800,000 silver last year. These figures include, in practically all

cases, the total cost for college and hospital. It is difficult to get a wholly accurate statement as some teachers volunteer their services, and in some of the budgets the salaries of the foreign teachers are not included. The two co-operative colleges receive annual grants from their respective provinces, Hunan and Kwangtung. The Hunan-Yale College is promised an annual subvention of $50,000 silver (of which amount $41,000 was paid in 1920); and the Kung Yee College also receives a regular grant from the Canton Government. In addition to these grants to colleges conducted co-operatively with the Chinese, the Mukden Medical College receives about $6,000 silver from the Provincial Government of Manchuria and the Medical School of Shantung Christian University receives an annual grant of $5,000 silver, unfortunately reduced lately to $3,000. Constant military activity in China during the past few years has hindered educational progress in many of the provinces; and yet a most determined effort is being made to fulfill these special contractual obligations, especially where foreign staffs are involved.

High rates cannot be charged for medical teaching for a long time to come, that is, in most parts of China. The Army and the Navy Medical Colleges provide free tuition for those who pass the entrance examinations; while the fees charged in other colleges range from a standard average of $20 silver a year, for tuition only, in the Chinese Government institutions, to $300 silver a year at the University of Hongkong. Board and room cost from $30 a year up. And even the moderate fees at most of the colleges, prevent many an able candidate from registering. Times without number have students come to ask for scholarship aid or for suggestions as to self-support even though the fee was only $30 per year. Such is the economic border line beside which a considerable proportion of students in China live.

How shall we evaluate the colleges that today are attempting to carry forward the torch of medical science? What of their resources? What of their ideals, their equipment, their teachers, their productive research? With few exceptions, they are attempting their task with far too little financial foundation. Is it not this in large measure that makes the visitor report: "Chemistry facilities are scanty and there is no evidence of proper apparatus for teaching physiology."

Or again, "The only laboratory is inadequate for a school with two hundred students." Or once more, "Equipment is scanty; and except for a minimum of practical instruction in chemistry, histology, bacteriology, and pathology, the teaching appears to be largely by lecture in the preclinical subjects."

There simply are no funds with which to provide more. A recent investigator writes in the Journal of the American Medical Association that the government schools are like houses built upon the sand; that they are subject to every passing storm of revolution and political intrigue. In not a few their success and existence depend upon the health and strength of the man at the head. The salaries of the teachers depend upon the personal influence of the director. Surely, such conditions are not conducive to a forward movement. Outside of the Peking Union Medical College, the only foreign institutions with a really adequate budget are the South Manchurian College at Mukden and the Medical School of Hongkong University. And I fear their Deans will not agree to this statement as to their sufficiency. With the huge incubus of soldiers that now lies heavy on the land, the Chinese group of colleges will have great difficulty in securing funds enough to keep alive during the period just ahead; while the foreign colleges not associated with governments are counting the cost anew. One, as has been stated, has decided not to continue. Two or three of the others look into the future in the hope that new funds will be forthcoming which will enable them to sustain and to increase their powers.

What of the standards in force? Only six as yet require thorough laboratory preparation in biology, chemistry, and physics. The Chinese colleges are still satisfied to admit middle school graduates. But there are indications of higher standards, for a pre-medical year is soon to be required in one or two of them. In ten of the twenty-four colleges, the course lasts five years. In Mukden and Hongkong this is because, very naturally, the British pattern is followed. In the Peking Union Medical College didactic work lasts four years but a year of graduate work is required before the degree is conferred. Changsha and Tsinan are sure to follow this plan, together with St. John's, as soon as their teaching staff is adequate. The government colleges are all "special medical colleges," since there

is as yet no Chinese university medical school, and these special colleges still follow slavishly the Japanese model for that grade, that is, middle school graduation plus four years of medical study as the requirement for a medical degree. The former German college, with its reputation for high teaching standards and excellent equipment, has been revived. A new dean and new teachers have reached the field; and the work to be done there is likely to place the school shortly among the stronger institutions of the land.

In the majority of the colleges the provision of lecture halls as compared with laboratories suggests that the imperative necessity of individual experimentation has not been sufficiently appreciated by the faculties. Belief in dissection is expressed everywhere, but actual provision for it is scarce. That physiology requires instruments of precision which every student must handle and that individual microscopes are needed by students throughout their courses is not fully realized, if one may judge by what he sees in most institutions. True, new laboratory buildings appear at several centers. Hangchow Provincial Medical College, for example, is to use its new buildings this autumn, but no anatomical laboratory with dissecting tables for every student is to be found there. The new college for women, also at Hangchow, consists essentially of recitation rooms. What gives one concern is not the simplicity of form or inexpensiveness of material in these new buildings, but the absence of any plan to let the student learn by personal experiment. The recently completed group of buildings for the province of Soochow and the group planned for the Board of Education College at Peking give promise of better provision, although in the former, even the new laboratories do not furnish space and equipment enough for each individual student.

In spite of the weaknesses mentioned, the teachers are on the whole a strong group. The Fellows of the Royal College of Surgeons in nearly every college where British take part and the corresponding Fellows of the American College of Surgeons in the institutions where Americans teach share the common task with French and Germans and Danes of distinction. Every college, however meager its budget or insufficient its staff, has teachers that would rise to high positions at home. In the majority of Chinese colleges, the

teaching staff consists largely of men trained in Japan. This is not at all unnatural when we remember what a stream of Chinese studied in Japan before 1914. It is nearer and less expensive to go there than farther abroad. Only a few of these teachers have had the opportunity to study in the Japanese universities. Most of them are graduates of the special medical colleges, whose standards and equipments are moderate. Japanese medical leaders have made such remarkable contributions to the science of medicine (one of their eminent research men occupies a prominent place on this program) that we have a right to look forward to the day when Chinese who study in Japan shall come into close relationship with the master minds of that country. We need furthermore to make sure that the men who go abroad shall be picked men, that they shall be placed under such influences as shall weave inextricably into the fiber of their being those ideals for which the leaders of the profession have striven. Otherwise, and it is unfortunately true already, too many of the returned physicians from Japan, from Europe, and from America, slip back and complacently accept lowered standards, become afraid of their own powers and prove eventually not an aid but a hindrance to the winning of confidence for modern medicine!

In research, the great field has been barely scratched. True, even from the earliest days, busy practitioners set themselves to wrest some secret from nature. Dr. Balme in his most valuable book, *China and Modern Medicine*, just published, divides the contributions into historical, anatomical, physiological, and clinical. To his record I venture to direct those who wish to know the facts. Logan of Changteh was the first to find *Schistosoma japonicum* in China; Goddard of Shaohsing discovered an important new fluke. Cochran found in Hwai Yuen that the Leishman-Donovan bodies of kala azar could be detected in the superficial lymph nodes. And what shall we say of the researches of Manson, Cox, Maxwell, and a host of other workers? In Peking the search for new truth has actively begun. To take one example, the recent observations on the parasites of Central China made by Dr. Faust during the past summer indicate how extensive is that single field.

A few statistics will prove illuminating. In China there are twenty-four medical colleges, or one for every 15,000,000 of the population;

in the United States there is one for every 1,250,000 of the inhabitants; in Canada, one for every 1,250,000. And the majority of these twenty-four colleges have slender resources, insufficient equipment, and an inadequate staff. In the entire country last June there were 2,050 medical students. This means only one student for every 175,000 of the population. In the United States there are 14,872 medical students, one for every 8,000. In Canada there is one for every 3,700 of the population. One thousand, one hundred and sixty-one physicians are listed in the 1921 directory of Chinese medical graduates, and perhaps as many more trained in Japan. Add to this 460 Western medical missionaries and the practitioners in a few large seaports, and the total number of physicians who are in a measure familiar with the principles of Western medicine does not exceed 3,000. Here we have 3,000 physicians, poor and good together, in a population of not less than 360,000,000; one modern physician to every 120,000 of the population. In Great Britain there is one to every 1,100; in Japan one to every 1,000; in Canada, one to every 1,050; and in the United States one to every 720. Measured in figures the record is pitifully inadequate, but measured in terms of influence, of uplift and awakening in the nation, "it is questionable," says Dr. Balme, "whether there has been any other agency at work in China during the past century which has done so much as the practitioners of Western medicine to gain the confidence and good-will of the people and to dispel that miasma of fear and suspicion which beclouded all intercourse between East and West in former years." Even after the first few years of Peter Parker's activity in Canton, Beadle was led to say of him that he "opened the gates of China with a lancet when European cannon could not heave a single bar."

Consider the move that is being made to extend government medical education. Partly through the plans of the Board of Education and partly through local initiative a program is being made that will include a medical college in every province. On October 22, 1912, in the very first year of the Republic, a law was passed regulating the establishment and outlining the curriculum for medical colleges.

Thinking people soon recognized that anatomical facts could not be guessed at. Pressure was brought to bear in Peking and in 1913 the Minister of the Interior made dissection legal. It is gradually be-

coming an available teaching method. Officials in every city and students in all schools must be taught to appreciate how indispensable such dissection is and must be led to create favorable sentiment.

In addition every hospital where earnest work is done is contributing to the progress of medical education. They are springing up everywhere; government hospitals, both civil and military; private hospitals and even community hospitals. None of these are more conspicuous in excellence of management and medical supervision than the Central and Isolation Hospitals in Peking.

Still another sign of the tendency to advance medical teaching is seen in the forming of a national committee on scientific terminology. This includes representatives from government institutions as well as missionary colleges and will soon put to flight the old confusion in nomenclature.

Again, medical associations, both local and national, are springing into being. Several of these are already issuing medical journals. True, much of this material is merely translated but original articles appear with increasing frequency. The journals of the Tung-chi College and the Tung-teh College in Shanghai are the most elaborate at the moment. Other useful journals are those issued by the colleges at Tsinan, Hangchow, and Soochow. Nothing more challenging has appeared than an article in the Soochow journal arguing for the extension of medical schools.

It is refreshing to discover, moreover, that increased financial support is being given to modern medicine. Over 50 per cent of the cost of upkeep of mission hospitals in China today is met with local funds, and 27 per cent of the hospitals meet all their expense locally, save for the salaries of the foreign staff. For the past nine years $300 a month has been paid with the utmost regularity to the St. James Hospital, Anking; and this grant is soon likely to be increased to $500 a month. The military government and the provincial assembly share the grant.

PRESENT ISSUES IN MEDICAL EDUCATION

What are the fundamental issues in medical education in China today? First of all, the arousing of a sense of need — the awakening of the popular mind to the distressing lack of trained men and

proper facilities for the care of the sick. We have already seen that the proportion of physicians to the population is 120 times as great in England and Canada and Japan as in China. Dr. Dewey is right, it is essentially a matter of transforming the mind of China. In the schools that responded to the inquiry of Dr. C. V. Yui, only 1,153 out of a total of 36,095 students indicated that they looked forward to the study of medicine. The leaders of public thought, educational authorities, pupils in schools, police magistrates, and all others who lead popular thought must be taught to recognize that a country's care for its sick and its program of preventive medicine is a public index of its advancement in modern civilization. Here lies the tremendous value of the public health program which Dr. Peter and his associates have been building up. They are arousing a public conscience and actually transforming the thought life of the community. More young people in high schools must be influenced to study medicine. Engineers are needed, but the proportion of those planning this career as compared with that of the physician is far too great. The responsibility lies heavy on teachers and other guides to hold before the young students of this land the opportunity for a life of service in medicine as compared with the life of business or engineering where the financial rewards seem greater.

The problem is largely a Chinese problem. The local educators and public authorities must be made to see the need. Only one-third of the colleges are mission colleges. The mission boards have entered the field of medical education. As we have already seen, theirs was the foundation on which modern medical education has been built. If their service is to be vital, to influence the methods and the standards of medical education in this great country, it must be increasingly effective. Every agency that is sending doctors to China must resolutely set apart more teachers for the medical colleges. Not by increasing the number of dispensaries where the foreigner can treat the sick himself, is China's need going to be met; but by an increased effort to train Chinese physicians, men and women themselves to minister to their fellow-countrymen and women. If missions are going to provide at all for medical education, they cannot afford to be so short-sighted as to attempt to increase the number of isolated hospitals when concentration of teachers in strong

groups at the teaching centers would make these institutions abound with vital energy that would kindle new life in the medical educational field of China. These students from China's own flesh and blood, and not physicians from afar, must be trained for service. Again, looked at from the point of view of missionary policy, no foreign influence can touch the life of an individual or a community in a measure that will compare with the influence of a Christian physician with wholesome professional standards.

Either the eight mission colleges must be greatly strengthened or some of them must frankly admit that they face the alternative of closing or doing second rate work. One has already done so. Eight years ago the China Medical Missionary Association voted that until a designated group of eight colleges had been made strong, no new colleges should be started by mission boards. Such restrictive votes are unnatural so far as they limit initiative or prevent sound co-operation. Those who are charged with the administration of mission medical colleges should at recurring periods make such an unselfish study, setting aside personal feelings, in order to secure for China as great a number of medical colleges as can obtain sufficient staffs and funds enough to do sound work.

The second great issue, closely related to the first, is that of high standards. For years Dr. Wu Lien Teh has been pleading for state control of education and practice. He has not had to go outside of China for his authority. Shen Tsung arranged for the establishment of medical schools in 1068 and his textbooks were prescribed by a central high medical court. The examinations were definite: one on the principles and one on the clinical practice of medicine and surgery; one on physiology and anatomy; one on differential diagnosis by the pulse; one on prescriptions and therapeutics; and one on the influence of air and stars. Those doing the best were given official medical positions, or were ordered to write or to teach; those of the second grade were licensed to practise; those who were unsatisfactory had to study their subjects again; while those who failed were ordered to change their profession.

With such an illustrious example in mind, Dr. Wu has worked for central control; and no more significant document has appeared on this topic than his Memorandum to the Board of Education in 1916.

Every teacher of medicine hopes he will live to see the realization of his ideals. At present there are no standards except those that individuals or single institutions choose to make. There is no one to prevent the failed third-year student, the disgruntled nurse, or the charlatan who steals a doctor's cast-off instruments and sets himself up as a practitioner, guaranteeing to cure all manner of outer ills, from claiming to be a doctor of medicine. Tuan Fang tried in 1908 to revive the licensure law of the Tsing dynasty imposing a $500 fine on those physicans who did not register; this refers, of course, to the physicians of the old school. He had 900 men examined and graded into five groups, the two lower being forbidden to practise. Do we suppose that they have continued to hearken to the prohibition?

What are we to do in these days of waiting? Every college, every teacher, must make it his personal responsibility to develop ideals and the power of sustaining them in every student. Every graduate must be aided to live up to the ideals with which he left his college. This can be accomplished in part by faithful advice as to the hospital where each graduate shall take his interneship, and later practise, in part by insisting that he read the literature, and in part by encouraging frequent visits to his alma mater and to other colleges. The colleges themselves must be kept as fountain-heads of inspiration. Among those who shape the standards the essential need is for leaders who shall face boldly the minimum requirements for maintaining modern standards in their particular centers, and for providing laboratory space for each student in every one of the fundamental branches of science; and who shall then either convince the authorities that sums must be provided to meet these expenses; or frankly admit that the school cannot live up to modern requirements. Gathered as we are in one of the most perfectly equipped and efficiently manned medical colleges in the world, our vision has already been broadened. We find ourselves reaching new conceptions of what the standards of a teaching institution should be. Remote though the time may be when other colleges can have a plant or a staff even distantly approaching the ideal set before us here, they may receive refreshment and be stimulated to fresh endeavor by the touch with Peking.

Consider for a few moments the service this college in Peking may render, nay, must render. In his Report of 1920, Dr. Vincent has already outlined a program. The college is (1) to give undergraduate medical teaching, (2) to provide in due time for graduate teaching, (3) to offer short courses for physicians, (4) to afford reasonable opportunities for the study of Far Eastern diseases, (5) to extend a popular knowledge of medicine and public health, (6) to promote research. But the aim is stated even more completely in two other brief phrases: "It ought to become *a rallying point* for medical training and research for the entire Far East"; and again, "*a station in the world-wide system* of medical education and research."

Let me venture, as one whose major interest is medical education in China, to indicate at this point, some of the special directions in which the medical world of the Far East may receive inspiration, at this station, this rallying point. Of course the primary aim of any medical college is to produce doctors. But fundamentally, this institution must uphold the spirit of investigation. I mean something far more than mere study into the nature and treatment of disease. Here should grow up the laboratory where inquiry will be made into the curriculum needed by the particular type of mind with which we have to deal in China. Here it will be possible to investigate the student himself, his attitudes and his responses to one and another type of teaching, his points of weakness and of strength. Chinese when well trained make good physicians and surgeons. We have all seen this in our wards and operating rooms; but they have not yet shown those qualities of imagination and initiative so essential in starting an independent growth. Nor have they developed that power to sustain which is indispensable in carrying on an enterprise launched with enthusiasm and abundance of initial support.

In Peking, then, we shall be able to determine the methods best adapted to our Chinese student. Here, too, the student will apply himself, by the experimental method, to the development in himself, and in his group, of those characteristics that are vital in forwarding modern scientific education. Such human research cannot be done abroad. The teacher in Peking will be free from the demands of practice and can give his whole time to the task. He will learn *how* to teach as well as *what* to teach his Chinese student, who comes of a

race in whom memory development is phenomenal, but whose entire method of study is henceforth to be in preparation for the making of sound and prompt judgments, for decisive and purposeful action.

Again, the teacher in Peking will discover how to modify his curriculum. We are all too prone to transport to a new field the recollection of what *we* were taught, to reproduce an arrangement of courses, a proportion of teaching hours almost identical with that which we learned somewhere else. But here in China economic conditions are different, climatic conditions are different: must we not make at this center investigations that will enable teachers throughout the country to formulate courses adapted to the local needs? Must not the *eye* receive a major share of attention? (Dr. Howard tells me that of all cases examined in Peking, 55 per cent have trachoma!) Will not parasitology, and its allied branches of helminthology and protozoology, claim a much larger share of time in the curriculum than in Western lands? The nervous system diseases of China have just begun to receive attention. When we think of the variety of nutritional and parasitic influences likely to have caused these maladies, we shall realize the emphasis they need and the abundant facilities necessary for those who undertake to shed light upon them.

And what shall we say of the vast field of pharmacology? Hardly a day passes without our hearing of some Chinese remedy of unusual potency, a drug that is reported as able to restrain the pernicious vomiting of pregnancy, a certain stone-like fungus that will expel round worms, a powerful diuretic, an herb that will reduce fever. For the trained pharmacologist, associated with the biological chemist and the botanist, the field of inquiry is infinitely large; and the psychological effect upon our Chinese friends, teachers and leaders of public thought as well as physicians, of such inquiry into the worth-while elements of the Chinese pharmacopeia, will be most surprising.

As regards investigation, here men will study how to adapt hospitals and dispensaries to the Orient, how to fit the laboratories to the needs of China, how to make them most serviceable in hot damp summers and cold dry winters. Here, also, we shall continue to study the food that the Chinese are eating, the nutrition their bodies need; and these findings will be made in the light of the economic condi-

tions we find in China. The chemist and dietitian and physician and nurse will meet in vitaminal fellowship with the student of economics and meteorology. In Peking, too, we shall test out matters still unsettled in the field of nursing. For here alone have we nurses enough to provide supervision for pupils in training. We shall know from the experiments here whether women nurses can be used in all the wards. The actual nursing needs of the group of hospitals throughout China have had to be met so rapidly since 1909, when the Nursing Association of China was formed, that there has scarcely been time for a laboratory study of the essential problems of adaptation.

"A rallying point" indeed! Not a place where the physical needs of the individual sufferer are to receive less attention than in a mission hospital, because this happens to be a center of research; but rather *more*. For *all* his needs, and the way in which they are to be met, can be studied here. His social setting, his economic status, his moral and religious nature, are to be ministered to here. In this connection I venture to point out that the newer methods being followed in this hospital by the Director of Religious and Social Work, should prove suggestive to every medical missionary. Without compulsory attendance at a traditional preaching service, friendship is extended in a personal way to each patient. As the result of such contacts there was a remarkable number of in-patients last year who voluntarily related themselves after leaving the hospital to the Christian community in Peking and elsewhere.

"A station in a world-wide system!" The hospitals established by medical missionaries throughout the land, which constitute both the advance guard in all outlying districts, carrying constantly farther the needs and spirit of modern medicine, as well as the foundation upon which medical education is being built, are looking to this institution. They are hopeful that the graduates leaving these halls shall be filled with the spirit of service rather than that of personal glory. At the present moment, it is difficult for graduates trained by European and American teachers to find their way into government positions. Such unwillingness to recognize these graduates occurs partly out of a temporary failure to appreciate that true medicine is all one and that those who are imbued with the de-

sire to seek truth must be given an equal chance to prove their worth. In the meantime, however, nothing is more essential than that graduates from schools with high standards shall be encouraged to serve in that same spirit of self-forgetfulness which characterized the early medical missionaries. If the hospitals in many cases lack facilities and staff sufficient to make them worthy practice grounds for our better graduates, let the institutions be strengthened; let each graduating student receive an impulse that will send him to them. Through these hospitals, particularly the mission hospitals, the spirit of modern medicine that is essentially the spirit of Christian ministry, can better be made known to China, can have a larger share in uplifting the masses, than by placing them in any other position. We must hope that many will also eventually find their way into government positions, but until these positions can encourage men to serve rather than to become self-complacent and self-seeking, we are in danger of ruining both the professional and moral fiber of those who graduate from our care.

In such measure as its facilities will permit, every medical college in the land must assume responsibilities similar to those which have been indicated for this model institution in Peking. At Mukden and Tsinan, at Shanghai and Changsha, at Chengtu and Hongkong and Canton, the same challenge is put before us. Grateful as every practitioner and medical teacher in China must be to those far-sighted Trustees of the Rockefeller Foundation who conceived and carried through the plan for this institution, the opportunity is now theirs, whether they are associated with government colleges or mission colleges, community hospitals or private hospitals, to relate themselves to it, to take advantage of the privilege of working within it, to co-operate with it, and together with its staff to develop a new basis for work in China and to generate, in fellowship, new inspiration for those whom we teach.

Time does not suffice to do more than allude to a very few other pressing questions:

1. The language through which medical instruction can best be given is still an open question; not perhaps as to the ultimate medium, but as to the time and the way for giving up English in a college like Peking; or, in the case of a college like Tsinan, as to the

method for increasing the ability to use English or some other Western tongue. The one essential is that the graduates shall relate themselves to the medical needs of their own people on the one hand, and on the other that they shall always live as students seeking continued contact with the productive minds of the medical world.

2. Relationships with the group of physicians trained in Japan must be made more cordial. Whether this shall be done by selecting them for our teaching staffs, either as regularly appointed instructors or as extra-mural lecturers, remains to be determined. There must be only one national medical association and good men must be given access to posts that need them, irrespective of the place of their training.

3. A method must be found by which more technical training can be provided for the army of assistants required in the hospitals of the land. There are 326 mission hospitals and 244 additional mission dispensaries in China, not to mention the scores of hospitals that have grown up through private or community initiative. In far too many of these the professional men and women are giving too much time to laboratory tests, to the mere mechanics of radiology, to bookkeeping and other administrative matters, to make it possible for them to do the work for which they are trained. Shall the medical schools set themselves definitely to training the technical assistants needed, or shall there be a new institute in some center not related to a medical college, where technicians and administrative workers may be trained? Graduates from such a school must be prevented from attempting functions beyond their powers, and, on the other hand, such centers must not draw away from medical colleges men and women who ought to be set apart for these teaching staffs. The awakened sense that better work is required than formerly makes the hospitals send out an appeal that their needs be met. Medical colleges must take the lead in meeting their demands.

4. A new program of pre-medical instruction must be drawn up for the whole country. Every medical college ought to turn over work of this kind to a college of arts and sciences, in order to free itself from the financial and administrative responsibilities involved and more particularly to give the student preparing for medicine the

stimulus and cultural background of college associations. Surely it is not a normal thing to take a student out of the middle school and to isolate him within the confines of technical training for seven or eight years. He must be thrown as long as possible with students and teachers that represent the variety and complexity of the life into which he is going later on. Colleges whose pre-medical science facilities are still inadequate must be made strong and enabled to take their share in a large plan which will train both for medicine and other sciences. In this connection a method must be devised by which the science work and the other departmental work of our colleges shall be described in such a way that each may understand what the other is doing. Some central committee or officer may be necessary to aid the scattered institutions to bring their work up to certain standards and to enable teaching staffs to understand each other.

5. The medical education of women is an issue already looming large in the Peking Union Medical College. The Pre-Medical School has now quite a number of women among its students. No sooner had Changsha thrown open its doors than inquiries were received and two women pre-medical students began work there last week. The same experience will be found throughout the land. There is a very strong feeling in some quarters that in addition to such facilities for co-operation in certain medical colleges, at least one medical college for women should be maintained. If funds and an adequate faculty can be secured there would appear to be no argument against such a move; but, in passing, it is worthy of note that the tendency to strengthen medical colleges exclusively for women is diminishing rather than increasing in Western lands.

6. A program for securing pupils to enter upon the study of medicine must be laid down. We must find in the middle schools throughout the country those which have mental breadth and initiative and win some of them for our profession. In his inaugural speech at Yale University last June, President Angell said, "It is obviously futile to look for intellectual leadership from men of second-rate capacity. * * * * No university is quite worthy of the name and none is serving to the full its own day and generation, that is not through its productive scholarship, enriching human life and en-

larging the borders of human understanding." Are we making an inclusive plan to find such minds for the medical profession in China?

FUTURE REQUIREMENTS

As regards the future, three things seem clear:

1. The future of medicine must be in Chinese hands. Medical missions alone can provide only scantily for medical education. Their finances and, in a measure, their aims, do not justify setting apart an indefinitely increasing number of men for this particular type of service. A single school like the Peking Union Medical College can inspire and lead, but can cope with only a small fraction of the need. Let every medical teacher, Chinese and foreign, bend his energies to the development of a national medical policy. On the one hand this will involve a central council to devise standards and examine candidates for licensure; on the other it will involve new co-operation by which Western workers will seek to adapt their contribution to the Chinese situation and will offer aid to the strengthening of Chinese forces, inspiring local leadership in province after province and putting upon it the responsibility for advance.

2. Only schools with high professional standards should be countenanced. For a time the product will be numerically inadequate, but will it not be inadequate even if we multiply our forces ten-fold or twenty-fold? Shall we not rather, whether government forces or mission forces, make the work that we do memorable for its excellence? Can we not devise, as the administrators of The Rockefeller Institute in New York have devised, a plan by which our work shall continually be held up and our leadership made to depend upon the character of the work we do?

3. The motive of our work must be continually restated. Hear the utterance of the President of the Rockefeller Foundation: "The greatest need of China is not, after all, for highly trained scientists, although they are essential; it is not, after all, for the greatest technical skill, although that is absolutely necessary if the great end is to be attained. But the great need of China is scientific knowledge and technical skill dominated by idealistic loyalty to the highest and best influences in human life; and that idealism that is most

enduring, that can be most counted upon, that is least likely to fail, is an idealism based upon a deep and abiding religious conviction."

"The profession of medicine," says Monsieur l'Abbé Huc in the record of his travels in China, "is considered an excellent conduit or waste pipe to carry off all the literary bachelors who cannot attain to the superior grades or pretend to the mandarinate; and China is consequently swarming with doctors, even without counting the almost innumerable amateurs." Those old days are going. We cannot afford to have amateurs any longer. To banish them wholly, we need a new consortium. It must be a consortium of medical educators from China and Japan and Europe and America who will take part fearlessly and with devotion in shaping the traditions of the profession. In leading new candidates into it, we, too, must have knowledge and skill and show that we ourselves are under the domination of a deep and abiding idealism.

MEDICAL EDUCATION IN THE DUTCH EAST INDIES

By

A. de Waart, M.D.

EARLY MEDICAL EDUCATION

Medical education in the Dutch East Indies was first started by the Government as a two-year course on behalf of the so-called "doktors-djawa," or Javanese doctors. Instruction was given in the Military Hospital at Weltevreden (Batavia) by military doctors in the Malay language. The aim was to provide a number of vaccinators against smallpox. But very soon facts showed that these men were often forced by circumstances to practice medicine to its full extent, on account of the insufficient number of properly qualified physicians. Therefore it was necessary to improve and enlarge the scheme of training.

In 1864 the original two-year course was lengthened to three years. In 1875 the course of study was divided into a two-year pre-medical course and a three-year medical course. At most, one hundred native boys, having passed through a native primary school, were to be admitted. The Dutch language was to be used for instruction in the medical course, as the Malay language showed too great a deficiency in equivalents for scientific, technical, and abstract terms. The number of military medical teachers was increased from three to five, and these were all only half-time men. In 1881 the pre-medical course was lengthened to three years. However, the members of the Committee for the final examinations repeatedly complained of the unsatisfactory results obtained, and continued to urge changes in the curriculum.

Of great influence upon the subsequent growth of the school was the government resolution of January 15, 1888. By means of this the temporary laboratory, which had been fitted up in the Military Hospital for the investigations on beri-beri by the Dutch professors, Pekelharing and Winkler, was made into a permanent one for pathology and bacteriology. At the head of this laboratory two *civil* medical officers were placed as director and subdirector, who were

to be at the same time director and subdirector of the doktor-djawa school. They were appointed in addition to the staff already existing; this meant an increased number of teachers, and gave also a greater stability to the staff, as those two members were not likely to be transferred. The director then appointed was Dr. C. Eykman, later professor at the Utrecht University.

However, teaching in the *native* primary schools proved insufficient for matriculation in the pre-medical school. So at the instigation of Dr. Eykman only native pupils of the *Dutch* Government primary schools, *where instruction started at once in Dutch*, were admitted to the pre-medical course (1890). The pre-medical course was reduced again to two years, which however proved later to be a mistake. In the same year, 1890, the practical medical and surgical training was greatly improved by providing accommodations for medical and surgical dispensaries in the military hospital.

REORGANIZATION

In 1896 Dr. Eykman was succeeded by Dr. Roll, whose reorganization proposals led to the following changes:

1. The alteration and enlargement of the existing rooms in the Military Hospital, so that the number of students could be increased to 150.

2. The building of a new school, a suitable site for which was found on the Hospital Road, using part of the Hospital gardens.

This new institution, where 200 students found ample room, was opened with due ceremony on March 1, 1902. The junior students shared the common lofty dormitories, the senior students had separate cubicles. A recreation hall was at the disposal of the pupils out of school hours.

The situation of the new school in the immediate vicinity of the military hospital made it possible for the out-patients, whose number greatly increased, and who received treatment in the dispensaries of the new school building, to be taken to the wards of the military hospital in case of need. Furthermore, it allowed the clinical classes to continue in the military hospital buildings, and, as before, the military doctors could retain their positions as half-time teachers.

In the military hospital the maternity ward for wives of soldiers was enlarged and material for practical lessons in obstetrics was ready at hand. It is a curious fact that, although everyone was convinced of the ignorance of the native midwives, still, up to that time, no obstetrics were taught at the school, and consequently the doktors-djawa were not qualified for this part of medical practice. Only a few didactic lectures on obstetrics had been given and the subject had been optional. In the year 1902, practical teaching of obstetrics was arranged, and it became an obligatory subject for the final examination. The graduates now received the degree of "Inlandsch Arts" (native physician) with full authority to exercise their profession as doctors in medicine, surgery, *and obstetrics*.

In the new school more care was bestowed on laboratory work in physics and chemistry as an indispensable foundation for the subsequent study of medicine.

3. The pre-medical course was again lengthened to three years. In order to be admitted the pupil had to pass through a Dutch primary school with a seven-year course; and in 1903, moreover, a matriculation examination was instituted.

4. An extra year was added between the third and fourth of the medical course in order to obtain more logical sequence in the order of the subjects. This made it easier for the students to follow the teaching, although the medical course was in this way lengthened to six years. Now for the first time general pathology was taught *before* clinical subjects. More time could also be given to the latter subjects, especially to elementary clinics in the fourth year.

5. Practical experience had shown that the measure, instituted on the advice of Pekelharing, to unite the directorship of the Laboratory and of the Medical School in one position was a mistake; it was impossible for one man to fill both posts at the same time and do the work properly. A special director for the school was therefore appointed in 1901. Moreover, the number of teachers was increased with five full-time men.

6. Furthermore, the course in legal medicine was improved with a view to requiring a high degree of efficiency from the graduates. Legal medicine also became an obligatory subject for the final examination.

The fact that since this reorganization the percentage of successful students rose from about 20 to about 48, or 8 per cent of the total number admitted in the pre-medical course, proves clearly that the new measures were greatly to the advantage of our medical education.

THE SECOND MEDICAL SCHOOL

In 1913 the Government of the Netherlands East Indies appointed a committee to advise on the question of a second medical school in order to increase the number of qualified physicians more rapidly. The advisers wished to accomplish this aim without lowering the standard of efficiency. In principle the Committee even wished to raise the standard in view of the great responsibilities and the large number of serious duties the native physicians were called upon to meet in their daily routine.

Following the advice of the Committee the second Netherlands Indian Medical School was opened in Sourabaya; and the schools at Batavia and Sourabaya were reorganized. Experience had shown that the first year of the medical course still produced unsatisfactory results. The cause of this was a hiatus between the pre-medical and medical instruction.

A so-called propædeutical class was therefore introduced as a link between the pre-medical and medical schools, now as a rule considered the first year of the medical course, which now consists of seven years' study, making the entire course *ten years after the seven years in the primary school.* The principal subjects taught in this propædeutical class are mathematics, physics, chemistry, and biology. It was rightly expected that the institution of the propædeutical class would facilitate the work of the students, since a sounder foundation was laid beforehand and the sequence of the subjects taught was arranged far more logically. For instance, physiology could now be started after very complete instruction in physics and chemistry.

We know from experience that under the present régime students get greater profit from their instruction, because the difficulties are brought more gradually within their grasp. The failures at the whole school and at the final examinations are fewer than ever before. *I must insist strongly on this fact because outsiders have often maintained that the course of study is too long.*

In 1913 medical study was *opened to students of all races*, including Europeans and Chinese; girls were also admitted, as well as students for free practice, paying fees and not bound by indenture to the Government. All graduates now received the degree of "Indisch Arts" (Indian doctor of medicine).

Laboratory work was placed on much broader lines. *Do things for yourself, see for yourself* — this should be the motto of all good medical education. There was no theoretical book-learning, but constant exercise of the perceptive faculty, the acquiring of deftness, perfect practical knowledge of instruments, and scientific methods of research, no acceptance of facts on authority, but independent personal investigation. Laboratory work was improved in all branches of study.

Very soon our buildings at the Hospital Road in Batavia became too small to accommodate the constantly increasing number of students and to provide at the same time sufficient room for laboratories. Sometimes in only *one* laboratory, seven teachers followed each other for practical lessons. No wonder that the preparations for these lessons presented enormous difficulties and that very little time was left for them, and neither time nor room was available for research work. Everyone connected with the school in Batavia looked forward to the possession of buildings, where the work of medical education could grow and develop without impediment or hindrance.

FURTHER PROJECTS

The late director, Dr. Noordhoek-Hegt (deceased in 1915), evolved a plan for the combination of new school buildings, with a laboratory of public health and the new Central Civil Hospital at Salemba (Batavia).

An entirely new group of medical buildings was projected and built.

In 1918 the Laboratory of Public Health; in November, 1919, the new Central Civil Hospital; and in July, 1920, the new medical school buildings were put into use. The arrangements in these buildings provide against all the difficulties we had to cope with at the Hospital Road. Our main building contains laboratories, museums, and lecture-rooms for physics, chemistry, biology,

physiology, physiological chemistry, pharmacology, and pharmacy, and also on the first floor classrooms for the pre-medical school. Over the principal entrance hall is built the aula, used for official ceremonies, awarding of doctors' diplomas, etc. In August, 1921, were held the full meetings of the Fourth Far Eastern Tropical Medical Congress.

Behind the main building is the building for anatomy, pathological anatomy, legal medicine, bacteriology, and hygiene, with laboratories, lecture-rooms, museums, and libraries for all these branches. Our large dissection hall for anatomy allows sixty students to work together, and is better equipped than that at any university in Holland. The autopsy-room and morgue are near the hospital.

The clinical lectures are given in a building in the center of the hospital grounds, reducing to a minimum the transport of the patients needed for demonstrations. The hospital wards now contain about eight hundred patients, whereas twenty thousand new patients last year came to the dispensaries. The senior students have daily to be in the wards and dispensaries, and get plenty of opportunity for bedside work, operations, etc. Laboratory work and Roentgen examinations are performed in special rooms in the hospital.

Our new operating rooms for surgery, obstetrics, and ophthalmology will soon be ready. Graduate work is being carried on in the clinical branches, especially by European doctors, studying tropical diseases. More and more native physicians are to be added to the teaching staff as assistants. The staff requires enlargement to give more time for research work, for which laboratory equipment in some branches is already quite sufficient; in others, for instance in physiology, there is still need of improvement. On the opposite bank of the River Tjiliwong, facing the medical buildings, will be erected up-to-date student-homes for 300 pupils.

PRESENT MEDICAL CURRICULUM AND ENROLMENT

The medical curriculum in Batavia is now very complete, none of the modern medical subjects is omitted in our curriculum. Last year we introduced an optional course in dentistry, improved our instruction in ear, nose, and throat diseases, and greatly enlarged our out-

patient work in obstetrics. In the pre-medical course English and German were taught as foreign languages. The school in Sourabaya will in due time have the same curriculum, but it has no residential system, and the buildings are not yet sufficiently equipped. They will, however, be ready in about four years.

There are now in Batavia more than 300 students of all races, male and female. Two hundred live in the dormitories, which are still in the old school buildings. They can pursue the courses at their own expense or be indentured to the Government. The indentured students enjoy free tuition and are provided with books, etc., free of cost. Moreover, they receive an allowance for food and dress. After obtaining their degrees they have to serve the Government for as many years as they have studied. They can, however, go into private practice if they pay back 650 florins for each year of study.

All graduates have the right to unlimited medical practice. Whenever they desire to have the same position in Government service as the Dutch doctors, they must first obtain their diplomas at a Dutch University. Twenty-three of our twenty-six graduates, who went to one, did this inside of only a year and a half. Dutch professors, with whom we are in permanent exchange as visiting lecturers, are very well satisfied with our students and graduates. In special cases fellowships are given for study in Holland.

(Here fifteen pictures of the medical buildings in Batavia were shown on the screen.)

I am very much indebted to your honored President, Dr. Vincent, who has made it possible for me to give this lecture. I hope it may be of some use in making a connection among the various medical educational institutions of the Far East. Without doubt the educational and practical problems we have to face are often the same, and mutual knowledge may lead to mutual help and better understanding. We shall be proud to co-operate with the brilliant and well-equipped institution which the Rockefeller Foundation is now starting in Peking, and to help each other in improving medical education, medical science, and public health in the Far East.

AN ADVENTURE IN PUBLIC HEALTH

By

George E. Vincent, Ph.D.

[an abstract]

Yellow fever, known for nearly two centuries, has been a scourge in Mexico, the West Indies, Central and South America, and has several times invaded the United States.

The discovery in 1901 by United States Army doctors in Cuba that yellow fever is transmitted by the bite of the female stegomyia mosquito; and the successful sanitation under General Gorgas, first of Cuba and then of the Panama Canal Zone, prepared the way for a larger campaign.

In 1916 the International Health Board of the Rockefeller Foundation commissioned General Gorgas to make a survey of the yellow fever situation with a view to organizing control measures on an international scale.

The Commission reported that the seed beds of the disease were relatively few and well known. A concerted attempt to eradicate the disease from these endemic centers was recommended.

After a delay due to the world war General Gorgas, in the autumn of 1918, was placed at the head of a special yellow fever commission to undertake a campaign of elimination.

He visited Central and South America, organizing in each country a national commission which served as a means of co-operation in a unified effort at control.

Meantime Noguchi of The Rockefeller Institute for Medical Research had made field investigations in Equador and Mexico, had isolated the germ of yellow fever, and had prepared a vaccine and a serum.

The principal attack was made under Connor in Guayaquil toward the end of 1919. This city had been the chief source of yellow fever for a century and a half. By July, 1920, the well-organized anti-mosquito work had freed the community of the disease.

Sporadic outbreaks and local epidemics in Central America, and a serious situation in Northern Peru were effectively dealt with by White and Hanson. Late in 1920 Mexico invited co-operation, so that the organization was completed.

Gorgas on his way to investigate a suspected area on the West Coast of Africa, died in London in July, 1920. He did not live to "write the last chapter," but he did see gratifying progress made toward the realization of his dream.

Political leagues are still causes of dissension, but there are hope and promise in a league for health which seeks to turn science from the arts of destruction to the healing of the nations.

METHODS OF VISUALIZING MODERN HEALTH IDEAS

By

W. W. Peter, M.D.

In China, where modern health ideas and practices have not been generally applied, ignorance and superstition are important factors. The methods I shall demonstrate have been developed gradually by the Council on Health Education since 1914, and constitute an addition to the usual methods of using literature, charts, posters, lantern slides, and moving pictures. They have been used in presenting the relation between national health and national strength to approximately six hundred thousand people.

PRELIMINARY ORGANIZATION

The following is the usual beginning. A small group of citizens in a community, desiring to begin improvement in health conditions in their city, appeal to the Council for help in conducting an educational campaign. A central committee composed of the leading officials, educators, business men, and missionaries is organized. In Foochow, 1,847 volunteers were enlisted. Two hundred and forty-seven meetings were held in one week, attended by 110,000 people, admission being by tickets distributed through schools, police officers, and churches. The purpose of that campaign was to fight cholera which manifested itself the previous year in about fifteen thousand cases. This executive committee pays all expenses ranging from several hundred dollars to $3,500 (in Foochow). The Foochow committee developed special methods, such as the use of a health parade with twenty-eight floats carried by coolies through 90 per cent of the streets of the city during one week. Each float visualized some one fact about cholera. But generally the backbone of the educational campaign is the demonstrated lecture, "Some Relations between National Health and National Strength." A translation of this lecture which follows indicates the simple, direct phraseology which has proved most effective:

THE LECTURE

Two Kinds of Citizens

Every community has two kinds of citizens. There are those who are well; they are like this lamp which is clean, provided with the right kind of fuel, and kept properly trimmed. Here is a model of a citizen of this kind. Then there are those who are sick. They are like this smoky lamp which is of no use to anybody. Here is a model of the second class of citizens. He has had smallpox. He has trachoma. He may have tuberculosis and quite likely has intestinal parasites. Impeded in this way he cannot get rich, take good care of his family, send his children to school, or be of any great help in building up this city. Every city has these two classes of citizens and their relative proportion determines to some extent the degree of happiness and prosperity possible in that city.

China's Load

[A poorly dressed man of diminutive figure comes upon the platform. He carries a heavy load, his back is bent and he walks very slowly.]

China is impeded in every step she is trying to take by an extraordinarily heavy load of disease. Every nation has its load of disease but in some countries sufficient attention has been paid to a study of the load to determine its exact nature and to discover ways whereby it may be lightened. Of what does China's load of disease, consist?

[The bag, tightly shut, disregarded for ages, is slowly opened. Huge blocks of wood are removed. Each one has characters written on four sides. There are blocks to represent smallpox, cholera, plague, typhus, hookworm, trachoma, typhoid, etc. Difficulty is encountered in removing some of the blocks like tuberculosis.]

Some parts of this load are exceedingly difficult to remove. If I were to bring in representatives from other nations you would see that not all of their loads have been removed. But it is a question whether the load of any one of them would be quite as large as this one for the very simple reason that in other countries the people are constantly at the task of lightening the load year by year, whereas in China we have not really begun in earnest. But if China is to become a strong nation this load must receive consideration; no nation can make permanent progress if it is thus impeded.

Death-Rates in Strong and Weak Nations

A famous Chinese sage has said, "the strength of a nation is its people." One way to measure strength is to ascertain how fast it is being lost. A study of strong and weak countries will reveal an astonishing fact. All strong nations have a low death-rate, and all weak nations have a high death-rate. I should also add that it is easier to ascertain the death-rates of strong nations because they make it a practice to employ trained men to do this kind of vital bookkeeping, while weak nations do not.

[From metal boxes suspended from a high rack on the platform hinged wooden plates are dropped. These plates are 6 by 8 inches in size. On one side white skulls are painted on a colored background. The first skull to appear is in profile and each additional skull approximates a front view. Thus the death-rates per thousand are visualized for England, Germany, and America, representing three strong nations. At the opposite end of the rack are boxes representing Mexico and India, with death-rates approximately double those first shown. In the center, between the strong and weak nations is a yellow box representing China.]

What is the death-rate in China? No one knows. It is said to be 40 per 1,000 per year! I have not placed China among the weak nations nor among the strong. It remains for you to determine her place in the future.

Relative Population

But some of you are thinking: "What difference does it make if China has a death-rate higher than most countries? We can easily spare those who die. We have a 400,000,000 population. China has too many people. A high death-rate is heaven's way of maintaining an equilibrium. It would be exceedingly dangerous to interfere by applying such modern health conservation practices as obtain in other lands. What should we do with all the people whose lives would inevitably be saved thereby? There is no room for them."

Is China overpopulated?

Let me try to answer only one part of this question, namely the actual population per square li (one-ninth of a square mile), as compared with other countries.

[Two tables are brought out. They are of the same size, about 4 feet square. One is colored red to represent Europe and the other yellow to represent the Orient. The tops of the table are perforated by holes, ten holes to a row and ten rows. The

holes cannot be seen because of the hinged tin tops. Underneath each hole, however, is the figure of a man. These figures are mechanically connected in series and can be made to appear on top of the table, being manipulated by the two uniformed assistants who work the levers and tilt the tables.]

First, let us ascertain the facts about Europe. The average population per square li is 13; Germany, 32; England, 40; Holland, 53; Belgium, 73. Turning to the yellow table, the average population for Asia is not 13 but 6; Japan, 28; India, 20; and China? According to a study of the Min Djen Bu Census and Custom's reports it is 11 per square li. It is said that with the development of her natural resources and modern methods of transportation, irrigation, and river control, forestry, and agriculture, China can support a population three times as great as now. At the present time China ranks tenth in density of population among the great nations of the world.

The Chain of Life in China

To allow present dangerous health conditions to continue constitutes a real menace to China. It does make a real difference to a nation if it disregards the presence of such serious diseases as plague, smallpox, typhus, cholera, when other nations are rapidly making practical use of the methods which have been discovered for preventing or controlling them. The strength and safety of China may be very easily effected.

[From the ceiling is suspended a long chain emerging from below a sky-blue curtain. The links are large, black, and strong. Opposite each link is written what this link stands for. Next to a huge box, painted a sickly white, is one link that is thin and partly broken. This is the present health link. The box represents the Chinese people. Nearby is a strong link waiting to be inserted to replace the weak health link. This is done by calling six men from the audience who hold up the big box while others change the link. The point is brought out that this change is possible only when all of the people understand what is going on and co-operate as far as possible. When the links are changed, an electric current is switched on and the powerful lights inside the box shine through the five-colored national flag.]

The change will not be as rapidly effected as this. But once the change is made the whole aspect of the country will be different. Now we have a chain composed of these links: favorable location, national longevity, natural resources, great population, industry, frugality, and public health.

The Human Body

In order to take proper measures for maintaining personal and national health it is necessary first of all to know something about the body in which we live. How many of you have ever seen a model of the human body? How many of you know the location and functions of the various parts?

[There is brought in at this point a model of the body, life size, with removable parts which are explained in detail according to the nature of the audience. There follows a full statement as to the purpose and place of medical schools, nursing schools, hospitals, and the teaching of health habits in schools as well as general health education among the people.]

The Largest Foundation Stone

What is the foundation of national health? What are the component parts making for national health?

[A glass box marked "National Health" is brought out and the audience is informed that once the important foundation stones are laid the box will light up. One by one the following stones are placed upon the platform; money, law, trained leadership, and finally public opinion. Upon placing them in pyramidal form upon the last mentioned, the top box becomes illuminated.]

Individual Versus United Effort

How is the foundation for national health to be achieved? The problem is so large and difficult. It will take so many years and so much effort that this is a very important question.

[A large board 7 feet high is brought to the platform. Its face is covered with green wheels in front of which metal figures are seen turning their respective cranks. These wheels are marked to represent the five classes of Chinese society,—scholars, farmers, laborers, merchants, and soldiers. Each member of these classes has to work at his own task to gain a livelihood. But on the outer rim of the board is a large yellow wheel on which are marked the characters for national health and national strength. This wheel barely touches each of the smaller wheels inside. All those connected with the small wheels then work at their cranks. Some work this way and some that. No one pays any attention to the large wheel. This apparatus represents individual effort.

A second board of the same size is placed beside the first. Here are the same classes but the people are touching elbows and working together. They not only move their own wheels but the larger one on the outside which is related to them all. This apparatus represents united effort. The two pieces of apparatus are worked for a few minutes and the audience is asked to decide which is the better way.]

China Tomorrow

Would you like to see a picture of China tomorrow after you have done your share in making a contribution to the solution of the health problem of the nation? You saw a picture of China today, overburdened by a load of disease impeding every step of the way.

[The curtains are drawn aside and a healthy Chinese is seen standing on the boxes marked plague, cholera, etc., which at the beginning of the lecture were in the bag slung around the neck of China. He holds the flag of China in his hand. On his back there is still a load of disease but it is smaller. The curtain is drawn.]

Now having seen some of the fundamental facts relating to this question visualized before our eyes, let us get down to the practical application in which we can all share now. The Chairman of the meeting will outline to you what you can do now for yourselves and for your own city.

A program of activities carefully worked out beforehand is then presented and an appeal is made for every citizen to give the project his support.

Before and after the public meetings the people are given an opportunity to see a health exhibit which is explained by previously trained students who constitute a "health faculty." Literature is distributed and announcements are made of further meetings in the various parts of the city.

SUMMARY

A summary of our experience in these campaigns follows:

1. Before modern health practices will be accepted by the Chinese people who do not understand them, general health education work is a primary necessity.

2. Because the Chinese and foreign conceptions on health subjects differ so widely, special methods have to be devised to interpret modern health ideals to suit the Chinese mind.

3. It has been found of some value to use three-dimension, moving apparatus built on a large scale with each piece of apparatus designed to visualize one idea. In the demonstration of this apparatus use may be made to advantage of well-known citizens in the audience.

4. After a general presentation of some of the relations between national health and national strength, a practical program with its special appeal to the local community should be presented.

5. Of permanent value in building up a better understanding of this subject are the large numbers enlisted in volunteer service and trained for leadership in this field.

BIOCHEMISTRY IN RETROSPECT AND IN PROSPECT

By

A. B. Macallum, Sc.D., F.R.S.

INTRODUCTION

In selecting as the topic of my address this evening the subject of Biochemistry in Retrospect and in Prospect, I have been influenced by my experiences during the last twenty years in explaining to many inquiring persons the significance of the term "biochemistry." They are, of course, familiar with the terms chemistry, physics, geology, and astronomy, for these, after more than a century of use, are now, as it were, household words, but biochemistry is a word of much more recent origin and its connotation is consequently much less widely known even among those whose general information is very excellent. Since this science, as a new-comer in the field of organized knowledge, can make its way successfully only by receiving the fullest support of those who are in a position to sway the opinion of the many, I think this is an occasion on which to present for general diffusion its significance, sketching briefly its history and indicating what I believe it will accomplish in the future.

This department of knowledge is known as biochemistry in the universities of the British Empire, as biological chemistry in those of the United States, and as Biochemie in those of Middle Europe. The name Biochemie was coined by Hoppe-Seyler in 1876 but it did not obtain general acceptance in Germany until about twenty years ago and his own Chair in the University of Strassburg was known as that of Physiological Chemistry, a title that is still used for the few professorships of this science which have been created in the German Universities, in the majority of which biochemistry is taught under the auspices of physiology.

BIOCHEMISTRY DEFINED: ITS RELATION TO OTHER SCIENCES

Biochemistry, briefly defined, is the chemistry of living matter and of all its products, normal and pathological, which are of the class known as organic. These include cellulose in all its forms,

cotton, and wood, the proteins which constitute silk, wool, and horn, and the products of tanning, but the scope of the subject as it is taught in universities is more limited.

Because living matter and a great many of its important products are colloids it deals with colloidal chemistry, and since it is concerned with organic compounds and has to take account of the physical condition of solutions, it covers some of the fields of organic and physical chemistry and physics. Further, as it is specially concerned with living matter it cannot ignore the science of biology.

EARLY RESEARCHES IN BIOCHEMISTRY

The province of biochemistry is, therefore, a large one. Indeed the fact that it is so closely associated with other sciences accounts for its rather late appearance as a distinct science. Colloidal chemistry, though it harks back to the researches of Thomas Graham in the fifties of the last century, did not begin to develop as a science until about thirty years ago, and physical chemistry had its beginning in 1887 with theories then advanced by Van't Hoff and Arrhenius on the nature of solutions. Biochemistry could not then have made great advances at a much earlier period even if its position as an independent or distinct science had been recognized. Further, certain great laws in the physical world had to be demonstrated as applicable also in the world of living matter. This demonstration involved difficulties which were only slowly overcome. The principle of the Conservation of Matter, though proved for the physical world by Lavoisier in 1790, was established for the animal body by Liebig about the middle of the last century, while the principle of the Conservation of Energy, enunciated by J. R. Mayer in 1842 and proved by the researches of Joule and others later, was only finally demonstrated as applicable to the animal body by Rubner in 1894. Without such conquests it would have been impossible to have made any important advances over forty or fifty years ago.

Nevertheless there were some notable conquests by chemists, physicists, and physiologists whose names should be remembered in the history of the science. This list includes Liebig, Wöhler, Gobley, Mulder, Claude Bernard, Fick, Wislicenus, Thudichum, Lawes, Gilbert, and Voit. These names are unfortunately now passing from

the record but from 1820 to 1880 they were honored as those of great pioneers in the trackless unknown. They are rarely mentioned in the text books today and one wonders sometimes whether the future will spare enough thought to keep them from the oblivion that now engulfs the great pioneers of an earlier age.

BIOCHEMISTRY DISTINGUISHED FROM CHEMISTRY AND PHYSIOLOGY

The period from 1868 to 1885 marks the time when biochemistry began to assert a claim to the control of a province of knowledge distinct from chemistry and physiology. It was the time of Hoppe-Seyler, Miescher, Maly, and Schmiedeberg. Hoppe-Seyler was a leader in the field whose service in the development of the science will always be recognized. From 1868 to 1874 he published four volumes, entitled *Medicinische-Chemische Untersuchungen*, in which were detailed the results of a large number of important researches in medical chemistry. In 1876 he founded the *Zeitschrift für Physiologische Chemie*. He was one of the first of those appointed to the professorial staff of the University of Strassburg, reopened in 1872, and his Chair was that of Physiological Chemistry, the first of its kind established. His standing as a physiological chemist made that University a center for all the students of the time who aimed to undergo a training and to obtain a point of view which would fit them for a career in research in physiological chemistry. For a few years they were not many, as one may gather from the fact that among the contributors to the first eight volumes of the *Zeitschrift* there were not more than eleven who had been students in his laboratory. The students of physiological chemistry elsewhere did not increase rapidly; in 1895, when Hoppe-Seyler died, the number of volumes of the *Zeitschrift* had reached only twenty.

Hoppe-Seyler vigorously asserted the claim that physiological chemistry was a science distinct from that of chemistry and from that of physiology. That claim was denied by the chemists and physiologists of the day, especially when the *Zeitschrift* was founded. In some instances the opposition was marked. Pflüger opposed the claim on the ground that its acceptance would do great harm to physiology. Many chemists were contemptuous. Hoppe-Seyler, however, persisted in his position and in the end won the desired recognition.

Students' Laboratory, Physiological Chemistry, Second Floor of Chemistry Building

Private Laboratory, Department of Physiological Chemistry

DISCOVERY OF THE NUCLEINS

Miescher, a student of exceptional ability and independent initiative, made his first appearance in research as the discoverer of the class of compounds known as nucleins, so called because the example of them which he isolated was derived from the nuclei of pus cells or dead white blood corpuscles. As we now know, nucleins are unique in that they contain nucleic acid which is a compound of phosphoric acid, a sugar of the pentose class and a purin or pyrimidin, the whole capable of uniting with a protein to form the complex nuclein which is the basis of the chief substance in the nuclei of cells and which is known to the cytologist as chromatin. The manuscript giving the results of his investigation Miescher offered in 1869 to Hoppe-Seyler for publication in the *Medicinische-Chemische Untersuchungen*, but the latter, considering that the results detailed therein were of too remarkably novel a character to permit of their going on record without verification, held it for two years, during which he repeated some of Miescher's investigations, finally publishing (in 1871) the paper with an accompanying note to the effect that he had verified some of the most important of Miescher's observations on the substance, nuclein, the discovery of which he regarded as one of the most signal achievements for a decade in physiological chemistry. I cannot help wondering whether today there is an editor of a scientific archive who exercises a similar circumspection in the selection of his material for publication, and also whether there has been evinced anywhere such an exhibition of the true scientific spirit.

The discovery made by Altmann in 1886, that the nuclein molecule contains an integer, nucleic acid, a phosphoric acid ester of special constitution, added to the significance of Miescher's achievement.

Miescher continued in later years his researches on nucleins which now began to have a special importance because of the discovery by Alexander Fleming in 1878 of the phenomenal processes of cell division grouped now under the term karyokinesis or mitosis, which is concerned with the equal distribution between two cells, arising by division from one, of all the chromatin in the parent cell. It was soon recognized that this chromatin is the carrier of all the distinc-

tive characters of the parent organism to the offspring and consequently the nucleoprotein which constitutes it has a special significance, not only from the morphological but also from the chemical point of view.

CYTOCHEMISTRY

In 1881 Langley had shown that the mother substance of some of the ferments, pepsin for example, could be localized in the cells of the peptic glands, and Heidenhain later demonstrated that zymogen granules exist in the pancreatic cells. These achievements, with the discovery and localization of nuclein in the cell may be regarded as constituting the beginning of the science of cytochemistry, a special and important line of biochemistry. They turned attention to the possibility of localizing in the cell, as seen under the microscope, some of its other products and contents, and in the eighties there were some who had hopes that the dawn of an era of great discovery in microchemistry had begun. It did indeed dawn but, although progress was made, the early light of that dawn is in great part still about us and the hope of a great achievement in microchemistry is still to be realized. The explanation for this postponement is the inertia which in the long run chills enthusiasm, for "hope deferred maketh the heart sick."

FURTHER LINES OF PROGRESS

Before the close of the century progress along other lines began with an impetus which has not yet spent itself. This was prompted by the interest awakened by the theories which Van't Hoff and Arrhenius advanced in 1887 on the nature of solutions, which put a new aspect on questions of osmosis, of diffusion, and of the absorption and secretion of inorganic solutes.

These theories accounted for catalysis, including ferment action, diffusion, and osmotic pressure, and they led not a few to believe that many of the vital phenomena could be explained on the principles of physical chemistry. As a consequence a considerable number of the younger generation of physical chemists entered as researchers the province of biochemistry in the two following decades, but although their contributions have been of value from their side of the subject it must now be recognized that physical chemistry,

as now defined, does not furnish solutions of many of the problems which confront the biochemist in his investigations of the phenomena of living matter, and it has been of comparatively minor service in explaining the processes by which living matter elaborates its products.

THE COMPOSITION OF PROTEINS

Perhaps the greatest stimulus to development which biochemistry received before the close of the nineteenth century was derived from the researches of Emil Fischer, on the composition of proteins, which were begun in 1893. The highest and most complicated products of living matter are proteins which, in a colloidal condition, form the physical basis of life. In the seventies and eighties of the last century the constitution of proteins was practically unknown. On digestion a number of them were found to form peptones which because of their diffusibility were supposed to be absorbed as such and to be reconstituted into proteins in the body. The decomposition of these peptones into simpler products, amino-acids, known as glycol, alanine, leucine, tyrosine, and one or two others, all of which had been isolated from the intestinal contents, was known in the seventies and eighties, but the significance of this was overlooked. It was even suggested that such products resulted from a wasteful decomposition in the intestine and that they were absorbed by the intestinal mucosa to undergo further wasteful decomposition in the body.

The Amino-Acids. Fischer, by subjecting proteins to hydrolysis by acids, with the aid of heat, obtained solutions rich in the bodies known as amino-acids, including glycol, or amino-acetic acid, alanine, or amino-propionic acid, leucine, or amino-isocaproic acid, and tyrosine. Some of these he succeeded in separating from each other by converting them in the mixture into ethyl esters and distilling, each ester passing over as a distillate at its own temperature. Fischer's methods were followed by a number of workers and through further improvements and the introduction of new and better methods the separation and estimation of the amino-acids which enter into the construction of the various proteins have progressed so far that we now know with an approximate degree of accuracy

the amount of each amino-acid in each protein. Further, we now know that the fundamental integer in each protein is an amino-acid, or, to put it more simply, the building blocks of the structure of a protein molecule in the great majority of proteins are amino-acids alone, and that the particular properties of a protein are due to the variety and the amount of the particular amino-acids of which it is constituted. As there are nineteen amino-acids it is obvious that an extraordinary variety of proteins is possible. Further, Fischer determined that proteins are really chains of amino-acids, each amino-acid present contributing a link in the chain.

How such chains can be constituted may be understood from the properties of a simple amino-acid like amino-acetic acid. This acid has the group NH_2 present in it and by virtue of its presence the acid has basic properties, that is, it can unite with an acid. It has also a carboxyl group, COOH, to which its acid properties are due, and it can consequently combine with a base to form a salt. Indeed the presence of both the amino and the carboxyl groups in the same molecule has suggested that they loosely unite with and thus partly neutralize one another and this, it is held, explains why amino-acetic acid is much less basic an acid than would theoretically be indicated by the presence of these groups.

Fischer succeeded also in showing how the amino-acids are linked in the proteins. In this linkage the OH of the carboxyl groups of one molecule and one H of the NH_2 group of another are eliminated and there results the union of the two molecules so affected:

$$NH_2CH_2 \cdot COOH + H_2NCH_2 \cdot COOH =$$
$$NH_2CH_2 \cdot CO \cdot NH \cdot CH_2 \cdot COOH + H_2O$$

As the product of this linkage has a carboxyl and an NH_2 group it can combine in the same way with two other molecules of amino-acids and the products, composed of four molecules of amino-acids, will, because of the presence of a carboxyl and an NH_2 group, combine similarly with two molecules of amino-acids. The process can thus be repeated almost ad infinitum, and theoretically the product might ultimately have so large a molecule that it could be seen with the naked eye and be picked up with a fine pair of forceps. Fischer succeeded by a tedious process in forming a polypeptide of eighteen

amino-acids. The cells of the animal body, on the other hand, have an extraordinary facility in the synthesis not only of polypeptides but of the highest and most complex proteins out of simple amino-acids, each organism, and perhaps each variety of cells constituting it, producing proteins of suitable types. It has also been established with some degree of certainty that the animal organism is not capable of forming any of the amino-acids, with the exception of the simplest one of all the nineteen, namely amino-acetic acid, and in consequence proteins like gliadin, which occurs in wheat flour, zein, which occurs in maize, and gelatin, all of which lack one or more of the higher and more complex amino-acids, cannot, if they are the only proteins in a diet, sustain life.

This work on the constitution of proteins has been paralleled by studies on the molecular structure of nucleins and nucleic acid. The results of these have indicated that the simplest nucleic acid molecule is a compound of phosphoric acid, a sugar either of the pentose or hexose class, and a purin or pyrimidin. The more complex nucleic acids are constituted out of the simplest acids, two, three, four, and perhaps more of the simplest uniting to form them. These nucleic acids have the property of uniting with proteins to form nucleins or nucleoproteins, a special variety of the latter constituting the all-important substance known to the histologist and cytologist as chromatin which, as already indicated, functions in the germ cells as the carrier to the offspring of the characters of the parent organisms. How it is constituted to function thus is as yet unknown but that is a problem the solution of which the future will undoubtedly bring.

RECENT INCREASED ACTIVITY IN BIOCHEMICAL RESEARCH

The work on the constitution of proteins as initiated by Emil Fischer and that of Kossel, Levene, and Walter Jones on nucleins and the investigations on the metabolism of proteins carried on from 1893 to 1908 excited keen interest among the younger generation of workers in science and led to a great accession of recruits to the ranks of the biochemists. As a consequence, the literature of biochemistry, covering all departments of this science, has increased enormously during the last fifteen years. Much of this literature is

to be found in the transactions of scientific academies and societies, but a not inconsiderable proportion of it has appeared in recently established journals devoted to biochemistry alone. A few statistics gleaned from an examination of these will indicate what activity now prevails among the biochemists. The *Biochemische Zeitschrift*, which began its publication in 1906, has this year reached its hundred and fifteenth volume. The American *Journal of Biological Chemistry*, started in 1905, has already completed its forty-sixth volume. Hoppe-Seyler's *Zeitschrift für Physiologische Chemie*, which began publication in 1876, and of which only twenty volumes had appeared in 1895, has this year reached its one hundred and twelfth. The total number of biochemical papers now annually published is very great. Early this year I endeavoured to determine the annual output by counting those listed for 1920 in the *Centralblätter* and in other journals for abstracting, and, as a result, arrived at the estimate of nearly four thousand for that year. This estimate I believe to be a conservative one. A large number of papers on biochemical subjects which have appeared in the medical journals and the publications of scientific societies are not included because a census of such journals and publications was, I found, too great a task.

All this activity is in marked contrast to that which existed in biochemistry forty years ago. The number of biochemical papers published in 1880 did not exceed one hundred and twenty; there was then only one journal devoted to their publication, of which one volume appeared annually. There were indeed other papers which touched on biochemical subjects, or contained the results of some investigations bearing on physiological or pharmacological problems which bore also on biochemical topics, but if these were counted one would also have to include similar papers in the estimate for 1920 and it would thereby have to be considerably increased.

Biochemistry has, therefore, very greatly developed since 1880 and it is, in consequence, asserting today a claim for recognition as a science of the first rank and promises supreme service in the solution of many problems which are of outstanding importance.

Its recognition as an independent department of activity is already conceded among men of science generally. The definiteness

of its knowledge after forty years of research and the value of that knowledge, not only to medicine but also to pure science, have been responsible for allaying opposition and silencing criticism on the part of chemists and physiologists of thirty to forty-five years ago. The only criticism that one hears today bears on the training that not a few biochemists have undergone, a training which, it is claimed, is one-sided or insufficient to qualify them for attacking the problems that have engaged their attention. This criticism is to a certain extent justified, but I may, however, state that the same criticism may be urged in the case of every science today, for there is in the ranks of chemists, physicists, geologists, biologists, and physiologists as large a proportion of inadequately trained workers as there is in the ranks of biochemists.

The past of biochemistry, because of the value of its achievements, is secure. Its future is to be one of still greater achievement. Indeed, it is certain that the activity in biochemical research will be greatly enhanced as the years go by, for the problems for investigation become more accessible and easier to attack with the increase of knowledge which the researches of each year bring. Further, the future training of biochemists for research will cover a far wider field than that which the present and the past generations underwent. This will enable our successors to obtain results where we have failed and to open up new lines of investigation, the results of which may lead to recasting our points of view on a number of subjects now apparently incapable of change. We have had an experience of such recasting in connection with the researches on "vitamines." Although the existence of such important substances was indicated by the researches of Lunin, in 1880, nothing came of his observations, and twenty years ago no one would have suspected that a diet of pure proteids, fats, and carbohydrates would fail to meet the requirements of normal nutrition. It was only in 1906 that the existence of these "vitamines," or "accessory food factors," was again indicated by the results of researches carried on by Gowland Hopkins. In the intervening fifteen years a knowledge of these substances has developed, in consequence of which they are now recognized as playing an all-important part in directing the course of nutrition — a fact that no one even suspected thirty years ago.

THE FUTURE OF BIOCHEMISTRY

Along what lines will biochemistry develop in the coming years? To answer this question with accuracy requires a prophetic vision which is granted to very few, and, therefore, I shall not presume to speak with any more certainty than is justifiable in one who has been a student in this line for the last thirty-five years and who has watched, expectantly, the progress of the science during all that time. I am confident that, in the main, its developments during the next thirty years will take place along the lines which I will now attempt to indicate.

LINES OF FUTURE RESEARCH

General Nutrition. The subjects of the research of today are certain to continue to be the subjects of patient and exhaustive research for four or five decades more. Among these problems are those involving general nutrition in health and disease. The disorders of nutrition are determining factors in a large number of diseases, and to control these factors more knowledge is necessary which can be obtained only by prolonged research on metabolism in health and disease. Our knowledge of the proteins, great as it is and due to the enthusiasm of the biochemists of the last twenty-five years, is still wanting on many important points. Our knowledge of the fate of the amino-acids resulting from digestion and absorbed by the intestinal mucosa is very incomplete and our conception of the nature of the transformations of the proteins which take place inside the body is exceedingly exiguous. Our knowledge, also, of the composition and mode of action of the various enzymes of the animal organism, especially those which are concerned in tissue metabolism, is very nebulous. We shall be able to obtain a full understanding of all such fundamental chemical changes in the various tissues and organs only through many and prolonged investigations.

Metabolism of Fats and Carbohydrates. A very great amount of research is still needed regarding the metabolism of fats and carbohydrates. We are yet in the dark as to the manner in which they are broken down in the tissues. The magnitude of our lack of knowledge may be illustrated by reference to the current explanation of the causation of diabetes mellitus. This disease has been, and still

is, held to be due to a loss of power on the part of the tissues of the body to utilize the sugar which is accessible to them. It is now becoming clear that there is in this disease a certain loss of power to break down fats, which shows itself in about 65 per cent of the diabetic patients of adult life by a more or less extreme adiposis and also in the production of aceto-acetic acid, β-oxybutyric acid, and acetone, which appear in the urine at critical stages and which undoubtedly arise from failure in the oxidation processes concerned in the final products of fat metabolism. There is still much research to be done on carbohydrate and fat metabolism before we can obtain a satisfactory explanation of the causation of even this one disease.

The Vitamines. The vitamines are today of surpassing interest in the biochemical world. The investigations of the last ten years have shown that these substances are indispensable in a diet which is to promote normal growth and maintain a normal nutrition. This is emphasized by the many thousands of cases of rickets among the children of Vienna at the close of the war, caused by the absence for two years of the fat soluble factors from their diet. The importance of the vitamines is also indicated by the prevalence of beri-beri during the last thirty years in Java, India, Japan, and in certain parts of China, the occurrence of scurvy from time to time during the last fifteen hundred years, and the incidence of pellagra in the southern parts of the United States, in Italy, Spain, and Egypt.

The full significance of the effects of the absence of vitamines from a diet has not been fully determined. McCarrison's observations on the results of feeding animals with vitamine-free food make one suspect that their action on the tissues of the body is more profound than the results of previous researches have indicated. The sloughing of the intestinal epithelium in his animals, but more especially the hypertrophy of the medulla of the suprarenal gland is, in my opinion, extremely significant. I am led to suggest that vitamines play a part in the animal body parallel in many respects to that of the internal secretions, although they are formed only in vegetable organisms. Are they internal secretions, the capacity to form which has been lost by the animal organism?

Their chemical constitution has still to be determined. The researches carried out on them have so far left their composition un-

determined. It is unbelievable that during the next ten years their chemical character will remain unrevealed; and it will fall to the lot of some biochemist to isolate one of them, very probably the antineuritic (water-soluble B) in a pure form and ascertain its composition. There should then follow its synthesis in the laboratory and the exact determination of its action in the body.

The Internal Secretions. Our knowledge of the internal secretions is still only fragmentary. We have definitely ascertained the chemical composition of that of the suprarenal gland, and it is possible that the compound thyroxin isolated from the thyroid gland by Kendall, may be the fundamental secretion of the gland, but we have no knowledge of the chemical characters of the internal secretions of the parathyroids, the thymus, the pituitiary, and pineal glands, or of the interstitial cells of the testes and ovaries. We are also wholly in the dark as to the character of the internal secretion or secretions of the pancreas that are concerned with carbohydrate metabolism, the absence of which leads to glycosuria or diabetes mellitus. Here is a field in which for the next two or three decades the activity of biochemists associated with physiologists may result in a lore that will enable us to control exophthalmic goitre, infantilism, acromegaly, diabetes mellitus, and other disorders due to the failure in activity, or to the hyperactivity of the endocrinous organs.

The Chemistry of Immunity. The chemistry of immunity to infectious diseases is today almost an unknown subject. The chemistry of bacteria has not been determined, largely because it is difficult or almost impossible to obtain a sufficient quantity of any one bacterial form to serve for such an investigation. The chemical characters of the substances which diffuse from them have not been ascertained and, in consequence, we know little or nothing of the mode of production of the antitoxins. The substances which can act as antigens are apparently of the protein class alone and therefore the antibodies produced by the antigens must be proteins. Their nature is, however, obscure or very indefinite; for, as Huntoon, Masucci, and Hannum have found, these antibodies, or antitoxins, or precipitins, do not undergo digestion with trypsin, and consequently, if they are composed of proteins, as they probably are,

these cannot be of the serum or of the tissue class. The character of the compounds that are responsible for the anaphylactic reaction is as yet a matter of surmise only, and therefore much remains to be ascertained in regard to them. The chemistry of immunology is a virgin field, awaiting the investigations of tireless and enthusiastic biochemists in the next few years. It is not too much to expect that in this line advances will be made which will add greatly to our armamentarium against infectious diseases.

The Chemistry of the Intestinal Mucosa and the Microchemistry of the Cell. Among the lines of investigation which will inevitably be pursued in the next few years and which I believe will yield results of transcendent importance will be those concerned with the chemistry of the intestinal mucosa and the microchemistry of the cell. The intestinal mucosa is one of the great gateways of the body to disease. It is constantly exposed to the action of products of bacterial fermentation, and when these are toxic the epithelial cells are the first to experience their action. In fact there are no other cells of the body which are subject to such an extreme variety of conditions and to such a constantly changing environment as are the epithelial cells of the intestinal mucosa. They undoubtedly react to a number of these conditions, neutralizing the toxic products and thus constituting the first line of defense of the organism against disease. When they fail to act in this capacity, disease consistent with its origin begins in one or more of the organs. I am strongly of the opinion that, for example, hepatic cirrhosis, several kinds of nephritis, arterio-sclerosis, angina pectoris, senile dementia, and dementia precox are due in part to alterations in the capacity of the epithelial cells of the intestine to perform their normal functions.

What changes the epithelial cells undergo to permit the development of the diseases mentioned we do not know. But we know very little regarding the activities of these cells.

The microchemistry of the cell, the other great line of advance in the near future, will involve an interest wider than that of medicine. The cell is the physical basis of life and consequently a profound knowledge of its composition, of the chemical processes that constantly occur in it, and especially of the physical forces that govern

it, would give us not only a deeper insight into the phenomena of disease but also some slight understanding of that great enigma, life itself. I have already indicated how little we know of the chemistry of the cell. Our knowledge of the physical forces is very much more scanty, in part because it is only recently that attention has been directed to them, but mainly because the working of some of these forces, even in the purely physical world, has not been fully investigated. This is especially the case with surface energy, which seems to play a dominant part in cell life. In association with another physical force, intrinsic pressure, it appears to control the absorptive, secretory, and excretory activities of the cell and there are some facts which seem to indicate that it is concerned in the most fundamental functions of nerve cells, such as the production and transmission of nerve impulses, in perception, sensation, and possibly memory and thought. This would postulate that the physical basis of psychic life is the co-ordinated surface energy of the millions of nerve cells in the cerebral cortex, the surface energy that is of the same character as that which determines the shape of a drop of water, the surface of molten planets, the sun, and the far-distant gigantic Arcturus. How the entity that is known as the Ego functions in this surface system of the nerve cells must remain a mystery.

It follows that the microchemistry of the cell involves profound philosophical problems as well as those of purely scientific interest. In researches along this line one comes into contact with questions which have formed the subjects of speculations ever since men began to attempt to solve the riddles of thought and being. Because it supplies a new approach to the solution of some of these the microchemistry of the cell will prove a lodestar to research in the coming years.

CONCLUSION

Biochemistry, therefore, because of its achievements in the past forty years and of its promise of achievements in the future, must be regarded as a development of knowledge of the first order of importance not only to scientific medicine but also to philosophic thought, even in its most esoteric form. During the next generation, biochemistry, associated with physiology and pharmacology, will

help to realize the hope that medicine will discard the last traces of that empiricism which has so long impeded its progress.

It is my earnest hope that here in China research in biochemistry will be generously encouraged and that in this great School of Medicine will be trained biochemists who will play an important part in fostering research in the various universities and medical schools in China, both those now existing and those certain to be founded in the coming years. There is, I am convinced, as much capacity for research in the young Chinese students as there is in the students of science of the Western World, and it needs only steady encouragement to develop that capacity to the fullest degree. If that encouragement is given and the expected results follow, this School of Medicine will have achieved one of its greatest functions.

Before closing I would pay my tribute to all those who have been concerned in the foundation of this School of Medicine. It is a magnificent achievement and it is certain to play a splendid part in the development of scientific medicine in China. This School is destined to be a great center not only for medical education but also for research, the constant prosecution of which will be a powerful force in combating the traditional ideas regarding medicine which exercise such an unfortunate influence on the minds of the people of this country. It is already a beacon light of hope to those Chinese who are longing for help to ameliorate the lot of the suffering among the swarming millions who are now, as in the past, subject, on an appalling scale, to the ebb and flow of misery, to famines almost countless in number, and to an incidence of disease without a parallel anywhere else on the globe. There is and will continue to be much sordidness in the world — we have seen much in the late war which would seem to deny hope to those who dream of the coming of a day when savagery will be washed out of the human mind — and there is, in consequence, a lessened optimism in all who work for progress. To find, however, here and there forces such as those which this great School will exercise, is to make us lift up our hearts in gratitude. And that gratitude will not die with us; in the far-distant years those who have striven nobly to serve their fellow-men will be remembered, and those who have made the establishment of this great School possible will be held in an abiding memory.

THE SEARCH FOR THE IDEAL IN HOSPITAL ORGANIZATION

By

S. S. Goldwater, M.D.

Sir Thomas More, the celebrated statesman and author, who added so much luster to the reign of Henry VIII, was struck by the fact that there was something about the hospitals of England in the early part of the sixteenth century that made men shun them, and in his famous *Utopia* he set forth the characteristics of an ideal hospital in a manner which has not been surpassed by any writer on hospitals, lay or professional, in the four hundred years that have since elapsed. In the perfect state which More's fertile imagination evoked, the people had a tender regard for their sick: "They take more care of their sick than of any others; these are lodged and provided for in public hospitals. They have belonging to every town four hospitals, that are built without their walls, and are so large that they may pass for little towns; by this means, if they had ever such a number of sick persons, they could lodge them conveniently, and at such a distance that such of them as are sick of infectious diseases may be kept so far from the rest that there can be no danger of contagion. The hospitals are furnished and stored with all things that are convenient for the ease and recovery of the sick; and those that are put in them are looked after with such tender and watchful care, and are so constantly attended by their skillful physicians, that as none of them is sent to them against their will, so there is scarce one in a whole town that, if he should fall ill, would not choose rather to go thither than lie sick at home."

With the best of good-will concentrated on hospitals in countries the most advanced in the arts of civilization, it has taken centuries of unflagging effort to lift hospitals to a position of safety and desirability. It was still a question sixty years ago whether the establishment of a hospital in such countries as England and France was an event fraught with good or evil, and hence we find Florence Nightingale beginning the preface of the third edition of her *Notes*

on Hospitals, published in 1863, with these words: "It may seem a strange principle to enumerate as the very first requirement in a hospital that it should do the sick no harm. It is quite necessary, nevertheless, to lay down such a principle because the actual mortality *in* hospitals, especially in those of large crowded cities, is very much higher than any calculation founded on the mortality of the same class of diseases among patients treated *out* of hospitals would lead us to expect."

If we may assume that hospital conditions in the United States during this period were not materially different from those prevailing in England, evidence of progress during the thirty years following the publication of Florence Nightingale's book may be found in the transactions of the National Congress of Charities, held in Chicago in 1895; for it was upon that occasion that Richard Wood, a Trustee of the Hospital of the University of Pennsylvania, remarked that there was still "among the uninstructed, a horror of the hospital," which Mr. Wood attributed to the fact that "the ignorant imagine the sick to be at the risk of untried remedies, and to be the subject of experiment, because poor and treated freely." But to Mr. Wood himself, and to the social and intellectual class to which he belonged, the hospital in 1895 had ceased to be a thing of terror, and had become "a tree of life, the leaves whereof are for the healing of nations."

In our own day the good accomplished by hospitals is not a subject of dispute; nevertheless, the precise place that the hospital should occupy in the body politic, the proper seat of responsibility for its existence and for its work, and the principles of its organization and administration remain fruitful subjects of investigation and debate. As an introduction to the consideration of means by which the usefulness of hospitals may be enhanced, let us review briefly some of the principal administrative objectives of recent times.

MODERN ADMINISTRATIVE IDEAS

About twenty years ago there sprang up in the United States an association of hospital superintendents, the first organization in the Western Hemisphere of men whose efforts were devoted to the improvement of hospital conditions. The declared object of the Asso-

ciation was the promotion of economy and efficiency in hospital administration. A review of the earlier transactions of this association shows that the hospital superintendents of America were at that time concerned chiefly with the care of buildings and the economical purchase and distribution of supplies. Hospital management was by them conceived to be scarcely more than a form of household administration.

How strikingly this point of view contrasts with that of the progressive superintendent of the present day, who, without relinquishing his interest in the problems of internal institutional management, is concerned lest the hospital fail to measure up to the health needs of the community! To define the relation of the hospital to the community is today accepted as the essential theoretical problem of hospital administration; to fit the organization of the hospital for the performance of its duties as thus defined, as its fundamental practical problem.

If the symptomatic treatment of disease in the individual no longer satisfies the scientific clinician, the mere sheltering of the sick in order that such treatment may be administered no longer satisfies the thoughtful hospital administrator, who seeks to bring organized medical practice under the influence of the latest and most approved scientific conceptions of disease. The path of scientific medicine proceeds through the several branches of pathology to causation and prevention, and it is along this path that organized medicine, represented chiefly by the hospital, is advancing. Numerous surveys undertaken by American communities in recent years clearly indicate this trend. The object of such surveys is to determine the character and the incidence of existing disease, and to disclose relevant environmental factors, and on this broad basis to define hospital functions and to formulate hospital programs. The logical result can be nothing less than an attempt to levy upon and skilfully to organize all available resources of society for the prevention and cure of disease.

That in one of its aspects hospital administration is a branch of domestic administration need not be denied, but orderly household arrangement is today regarded as the least of hospital problems. The hospital has become conscious of its duty as a center for medi-

cal research in preventive as well as in clinical medicine, as an instrument for the training of physicians and nurses, as a school where the laws of health may be imparted to the laity, and even as an avenue by which statesmen may be led to perceive the danger of any social or industrial system which disregards the health of the people.

John Morley in his *Life of Voltaire* tells of Voltaire's youthful intellectual limitations under the narrowing influence of social life at the court of France; he describes Voltaire's escape into England and indicates the enlightenment which resulted from Voltaire's challenging and stimulating contact with a free people and their institutions. When Voltaire returned to France, says Morley, he "had tasted of the fruit of the tree of scientific reasoning and had become alive to the central idea of the social destination of all art and of all knowledge." Intellectual and social influences no less potent than those which influenced Voltaire's later career have recently been at work to widen the horizon of the hospital administrator and to reveal to him the social character and destination of the institution over which he presides.

TYPES OF MODERN HOSPITALS

The three great types of hospitals in the modern world are the public hospital, managed by public officials and supported wholly by public funds; the private, non-sectarian hospital; and the sectarian hospital, likewise under private control. Each of these types has distinctive characteristics, but all reflect in greater or less degree the scientific, social, and economic standards of the period.

The private or voluntary hospital, upon which the people of England pride themselves as peculiarly an English institution, is dominated by the belief that bureaucracy, with all that the term implies of the inflexible and unpitying application of rules, lack of initiative, and loss of spontaneity, is the worst of all possible influences in a humane institution, and the last of all possible forms of control which should be tolerated by free men. The English system, transplanted in America and in the British Colonies, has flowered vigorously, but neither in the overseas dominions of Britain nor in the United States has there been such uncompromising insistence as in

England on absolute freedom from all subordination to or official relationship with government authority.

Generously supported by voluntary contributions, while neighboring rate-supported or state hospitals were receiving insufficient doles from the public treasury; free to experiment with both construction and organization, while public hospitals were fettered by official restrictions; so situated as to be able to take a leading part in medical and nursing education; giving generously to the poor and deservedly applauded as an expression of the more kindly qualities of the Anglo-Saxon race; limited in size and therefore free from the evils of machine-like administration which cling so tenaciously to great institutions, the voluntary hospitals of England were long regarded as the supreme charitable effort of modern society at its best. Nevertheless, the English voluntary hospitals, compared with voluntary hospitals in other parts of the English-speaking world, have seemed to some to be mistaken in their refusal to utilize any of their facilities for the treatment of the well-to-do, as well as in their uncompromising determination to steer clear of official control. The traditional English policy has apparently delayed the day of hospital co-ordination, without which a comprehensive community program for the conservation of health cannot be achieved. Just now some of the hospitals of England seem disposed to reshape their program so as to provide service for social classes heretofore excluded from their benefits. A drift of policy is likewise discernible in the direction of partial state support.

In the United States voluntary hospitals have been widely developed along sectarian lines. The religious instinct, often suppressed under the stress of modern economic life, is apt to reassert itself when illness appears. The sufferer who is racked in body and mind finds peace most readily among fellow-believers. Eager to render service, the churches of America have vied with each other in the endowment of sectarian hospitals where service is offered alike to rich and poor, and where tender nursing care and a sympathetic religious atmosphere are regarded as of greater worth than mere efficient business organization or even, may I say, than accuracy in diagnosis.

In the types of hospitals which we have just been considering,

Kitchen for the Preparation of Chinese Food

Public Ward, Department of Medicine

Laundry, Second Floor of the Power-House

Engine-Room with Dynamos, Pumps, Air Compressors, and Refrigerating Machinery

ideals of freedom, sympathy, and religion determine to a great extent the general character of the hospital, and fix the nature of the controlling authority; but there are countries where these motives do not freely operate, sometimes because the underlying human instinct is not sufficiently developed, sometimes because means are lacking, and again on account of political conditions. In the latter connection, one thinks of continental European countries where organized medical service, originally almost wholly an affair of the church, has become an accepted function of the state. Even in those parts of the world where the voluntary hospital, sectarian and nonsectarian, has flowered most luxuriantly, the insufficiency of available private funds, the tendency of voluntary hospitals to focus their attention on certain classes of the sick to the exclusion of others equally deserving, and the imperious demands of social hygiene, have caused the state to set up public hospitals for the purpose of filling gaps in the voluntary system.

There are two respects in which the state hospital occupies a position entirely distinct from that of the voluntary hospital; the first is its acceptance of the responsibility of society as a whole (in contradistinction to that of sectarian or other groups) for medical relief; the second is its support, at least potentially, by all the resources of the state. There is no limit to the share of its wealth that the state may devote to the protection of the health of its citizens, and there is no social or invalid class which may logically be excluded from the benefits of a state medical service, once instituted. The principle of state responsibility for the care of the sick having once been accepted, the extent of its application becomes simply a question of expediency. In its narrowest application, state medical service is limited to the care of persons suffering from communicable disease, and here the dominant motive is the protection of society, rather than the care of the sick; in its widest application, it includes not only every useful variety of hospital, but, reaching out beyond the walls of the hospital, it seeks to provide medical treatment in the school, in the workshop, and wherever such treatment may be required, even to the extent of providing constant oversight of the health of citizens, in all the circumstances of life, from infancy to old age.

DEVELOPMENT OF CLINICAL ORGANIZATION

While the progress of a hospital toward efficiency may be accelerated or retarded by its status as a public or a private institution, social, scientific, and economic forces play upon all types of hospitals without regard to their official relations. Perhaps the greatest single factor in modern hospital development has been the specialization of labor, a process which may be observed both in the medical branches and in general hospital administration. The intensive cultivation of limited areas of thought and action is a phenomenon characteristic of our age. It has left its impress on all the sciences and on most of the arts, but in medicine its first strong impulse has now been expended, and the period of differentiation, which tended to separate medical practitioners into many classes, has been followed by an irresistible demand for the co-ordination of the efforts of the different types of practitioners. Thus we have arrived at so-called "group medicine."

In the earlier days of specialization, specialists in New York and elsewhere sought to acquire the facilities necessary for the free development of their art through the establishment of independent hospitals of limited scope. They were forced to do this by the refusal of the departments of general medicine and surgery to yield ground to them. For a time the internist and the general surgeon were able to maintain their opposition to clinical innovations. But the specialists working in hospitals of their own, outside of the general hospitals, progressed rapidly in the development of an invaluable diagnostic and therapeutic technique, and it was not long before the need of their services began to be felt in the general hospitals; at this time consulting specialists were added to the regular hospital staffs. These consultants were at first simply called in occasionally to assist in diagnosis and treatment, but in the course of time the hospitals perceived the advisability of providing separate wards together with suitably equipped treatment rooms and laboratories for the special clinical branches; and thus the departmentalized hospital emerged. The change that we have just outlined was most quickly effected in hospitals which were affiliated with medical schools, for it was in such institutions that the need of varied and comprehensive clinical facilities was first experienced.

One of the things that stimulated the development of hospitals made up of a number of medical departments, combined and co-ordinated in such a manner as to permit of concerted clinical effort, was a growing appreciation of the fact that, indispensable as may be the specialist's contribution to the welfare of the hospital patient, it is prudent not to regard this service as self-sufficient or final, but wise rather to estimate it as a link in the chain of co-operative clinical relief. The time is rapidly approaching when specialists will not be willing to treat most of their patients unaided, and when public opinion will decline to sanction such treatment, even if the specialists be willing.

Disregarding for the moment the personal equation and considering merely the question of method, one may today with reasonable accuracy appraise the clinical proficiency of a hospital by ascertaining the number of separate departments which contribute to the diagnosis and treatment of the average clinical case. If it is not always true that sound practice prevails where team work flourishes, at least we may say that the opportunities for effective medical work are greatest where team work is highly prized. Broadly speaking, then, it may be said that a notable advance has been made toward hospital efficiency, first, by the training of special types of practitioners, and then by the co-ordination of the activities of the several skilled groups.

LABORATORY DEVELOPMENT

While the clinical development of the hospital was proceeding along these lines, laboratory medicine was following a parallel route. The single pathologist who, thirty or forty years ago, was able without an effort to satisfy all of the scientific demands of his clinical associates, has been replaced by a numerous laboratory staff, each member of which finds plenty of work to do in his chosen specialty, whether it be tissue pathology, bacteriology, pharmacology, serology, radiology, or cardiology, but in this field also the attempt to achieve perfection by intensive specialization has been followed by a growing appreciation of the dangers of isolation, and by a demand for a close working arrangement between the laboratory and clinical groups.

The successive phases of laboratory development are reflected by the manner in which hospitals have planned and erected their laboratories. An historical study of hospital plans tells the whole story. Beginning in 1870, when hospitals were frequently planned without laboratories of any kind, one finds in succession the following laboratory types: a single, rather small room; a small pathological laboratory combined with the morgue; a larger laboratory, equipped for pathology and bacteriology, still combined with the morgue; suites of rooms in the arrangement of which chemistry finds a well-recognized place, but which, despite a growing intimacy with the clinical departments, continue to be located in basements or in other remote places; differentiation of the general from the clinical laboratory, the latter becoming an important annex to the ward; and finally, a stage in which the intimate collaboration of the laboratory and clinical divisions of the hospital is recognized and promoted by the grouping of the wards and the out-patient department about a central building, which contains all that the hospital is able to afford in the way of specialized diagnostic and therapeutic equipment.

CONDITIONS OF PROGRESS

About thirty years ago, a feeling of restlessness swept over the hospitals of the United States and Canada. Under the leadership of a few men of genius, magnificent work was being accomplished in one or two centers, and a standard of achievement was thus set up which stirred others to action, prompting widespread reorganization. But how to proceed was a problem; for, in many instances, when a new scheme of organization was proposed, it became apparent that the key positions in the clinical organization of the hospital were held by men not abreast of the times, and that no matter how the organization might be changed on paper, the result was likely to be the reinstatement of some of these influential men in positions directly athwart the path of progress. In this situation the conviction grew that youth with its modern training would save the day, and, in order to create positions for young men of promise, a plan was widely adopted for the automatic retirement of the incumbents of clinical positions upon reaching a certain age, or upon the completion of a definite term of service. America was at least thirty

years behind England in resorting to this expedient. French sympathy with the idea that men of mature years involuntarily impede progress is somewhat touchingly expressed by Duclaux who, recounting in his study of Pasteur the difficulty experienced in obtaining a hearing among medical practitioners for advanced biological conceptions, says: "Physicians are those I would wish to lay hold of, and I begin to fear that I shall not succeed. I know very well that old physicians do not read any more, and that when they do read, do not understand." Although, here and there, a useful hospital career has perhaps been cut short by the policy of systematically replacing older with younger men, the net result has doubtless been advantageous to progress; but so simple a rule of procedure does not and cannot of itself invariably bring about an ideal hospital organization. Let one clinician be replaced by another, and if both have the same outlook on life, even though one be old and the other young, the same stagnation will result. How to insure perpetual progress is the problem.

Is the problem automatically solved when teaching is introduced? Is teaching the magic word? I need but recapitulate the familiar arguments in its favor. To the teacher, surrounded by the eager and inquiring minds of youthful students, is given a sure and constant incentive to discover and rediscover truth. The mind of the teacher is perpetually refreshed. The conscientious and well-endowed teacher can hardly fail to become observer, thinker, questioner, leader. To him is given the opportunity, through his influence upon the minds of his students, to project himself indefinitely into the future. In the atmosphere of the school, research is born, and research is the key to the hidden secrets of nature. Thus the greater usefulness of the teaching hospital is apparent. But all teaching hospitals are not alike in their organization; standards are lacking, and appear to be needed. We arrive then at the question of hospital standardization.

HOSPITAL STANDARDIZATION

Can a type of organization, a method of hospital administration, be prescribed which is suitable for all places and all times? It may be useful to formulate the principles of hospital function and organization, but to define in exact terms the character of the organiza-

tion, and to limit the activities of the hospital within the terms of the definition, is to obstruct progress. Standardization so conceived is a more pernicious influence than state control or bureaucracy, for a bureaucrat may change his mind, while the written word is inflexible. Nevertheless standardization becomes a useful instrument when understood simply as a means of upholding minimum standards.

The standardization of hospital work is no novelty. Standards exist wherever the state through legislation has defined the conditions under which medicine or nursing may be practiced in a hospital. The formation of voluntary organizations for the promotion of standards beyond those thus prescribed by the state is an indication that there exists a professional or popular demand for safeguards not yet required by the authorities. Such a movement, expressing high ideals, stamps as substandard the hospital which does no more than conform to the modest requirements of the law.

In a large country, where educational and social conditions are not uniform, the highest standards cannot be widely established or uniformly maintained either by law or by voluntary associations, but conscientious effort to determine and define those things which are the indispensable attributes of honest scientific work, for example, accurate records of clinical and laboratory observations, may be extremely useful. Standardization thus conceived encourages inspection and publicity, and keeps alive a sense of responsibility; it promotes a healthy rivalry among hospitals, and generates a demand for better things.

IMPORTANCE OF THE HOSPITAL PLAN

The consideration of the basic principles of hospital planning is relevant to the present discussion; for while anywhere and under any physical conditions the competent and resourceful physician will find a means of helping his patient, a hospital in which many physicians are employed cannot function smoothly in the absence of a sound physical basis for its operation. The plan of a hospital suggests, and to a certain extent influences, its development, its organization, and its methods of work. Serious attempts have been made to insure perfection in hospital organization by means of hospital

planning, but it is evident that the physical arrangement of a hospital which is planned and erected at a given moment in the history of medicine, cannot do more than meet the requirements of that moment. The hospital which is complete today is inadequate tomorrow. The most that can be done in the planning of a hospital is to satisfy, after careful inquiry, all the demands of the period. A constant need of all hospitals at all periods is the need of change, and the most important single principle in hospital planning is undoubtedly the principle of flexibility. Other important principles of planning are unity, diversity, hygiene, and economy, to each of which brief attention is due.

1. Unity. Modern medical treatment involves a wide variety of diagnostic, therapeutic, and nursing procedures, and an elaborate domestic economy. A well-ordered hospital necessarily contains many clinical and other subdivisions; the specialized character of these subdivisions readily suggests the splitting of the hospital into many parts and hence the architect is apt to be led away from the fundamental idea that the hospital is an organic unit, which cannot function vigorously unless all of its departments work in harmony; but upon the due recognition of this principle of unity the successful operation of the hospital largely depends.

2. Diversity. A glance at hospital activities at once discloses many diverse functions. There are patients to be cared for in bed and out of bed, indoors or out of doors, singly or in groups, in delirium or in convalescence. There is food to be prepared and distributed; there are linens to be washed, dressings to be sterilized, accounts to be kept, valuables to be stored, visitors to be received, nurses to be taught, housed, fed, and provided with opportunities for recreation; there are operations to be performed, X-ray examinations to be made, refuse to be destroyed, coal to be stored and burned, animals to be housed, culture media to be prepared, chemical analyses to be performed, postmortem examinations to be made, funeral rites to be conducted; and the hospital building must lend itself to the convenient performance of all of these tasks. Certain principles of orientation and arrangement are valid, respectively, for particular departments of a hospital. If the architect considers separately each distinctive function and plans for it appropriately, a variety of

structural outlines will emerge. If he then proceeds to build for each function, regardless of its place in the general scheme, chaos will result. While the value of diverse forms must be recognized, the necessity of combining these forms into a practicable unit must not be overlooked. On the other hand, if a plan is adopted which is too simple and which is selected on account of its correspondence to some particular hospital function, the resulting building may be satisfactory in part but will not give satisfaction as a whole.

3. Flexibility. A hospital building, in which the qualities of unity and diversity have been happily blended, may be a perfect instrument at the time of its completion, but, as I have already said, unless a certain measure of flexibility is added, the building will not long serve as a perfect instrument. Social changes, community growth, scientific discovery create new demands which every hospital is called upon to meet. Healthy hospitals are growing hospitals, but their growth is not necessarily symmetrical. New discoveries are constantly opening up new lines of medical treatment which call for additional space-consuming therapeutic apparatus. Nursing standards, and the methods of recording work done are forever advancing. A hospital which begins as a medical boarding house is eventually called upon to participate in health education, in the clinical training of medical students, in postgraduate medical teaching, in scientific research. A sudden windfall enables the hospital to enlarge some clinical department or to establish a children's health center. Pressure is constant, both from within and from without, and the hospital must be in a position to accommodate itself to every reasonable demand.

4. Hygiene. Hygiene is the most vital of all principles in hospital planning; a hospital which is not rich in health values is a failure. Health values in hospital construction do not reside exclusively in smooth walls, smooth floors, and rounded inner corners, but include certain features or characteristics which tend directly to the promotion of health, such as the proper orientation of wards, the sun exposure of balconies, roofs, or other outdoor space accessible to patients, effective ventilation, quiet bedrooms for night nurses, proper dormitories and recreation rooms for all resident officers and employees, a cheerful and tonic outlook; and also features which

aid in the prevention of disease, such as receiving wards, quiet rooms, isolation wards, sterilizing equipment of many kinds, and sanitary construction.

5. Economy. It is a mistake to consider building cost apart from maintenance cost. Broadly speaking, economy of use is more important than economy of production. A metal door frame may be cheaper in the end than one of wood, a tile floor in the final analysis may be cheaper than one of composition, a white metal faucet may be cheaper than a red, a copper cornice cheaper than one of galvanized iron. Durability is not extravagance. Extravagance in hospital construction resides in excessive decoration; in the use of costly materials which are not durable or easy to care for; in waste of space. Generally speaking, a concentrated institution is the cheapest to build and to operate, but in our discussion of the diversity of hospital function we saw that extreme concentration and simplicity of design ultimately defeat their own ends. An economical hospital is one in which every cubic foot of construction gives maximum prolonged service.

Systematic consideration of the details of hospital planning would be somewhat out of place in the present discussion, but I may at least be permitted to emphasize how indispensable to efficient work are wards in the planning and arrangement of which due consideration has been given to the personal comfort and the privacy of patients, to the requirements of case grouping for purposes of study, to the value in certain disease conditions and in most climates of treatment out-of-doors, to the need of suitable examining and treatment rooms, to the installation and placing of the apparatus which modern nursing service demands. Outside of the wards, apart from the always present and indispensable kitchen and laundry, the heating, lighting, and power plant, and the business offices, departments which on account of their intimate relation to the clinical and scientific functions of the hospital and to staff efficiency call for the most careful consideration in hospital planning, are the admitting and social service departments, the out-patient department, the diagnostic and research laboratories, various therapeutic departments, diet kitchens, record rooms, library, teaching rooms, and residential quarters for doctors, nurses, and others.

GENERAL CONSIDERATIONS

Lack of time forbids any attempt to examine at length the details of the medical, nursing, and business administration of the hospital, but I wish to record my conviction that in the field of acute diseases the general hospital in which the clinical specialties are combined, and in which alone a proper co-ordination of effort can be secured, is preferable to a multitude of separate specialized hospitals, or to a loose aggregation of independent institutes which favor isolation and which afford no automatic corrrective for the mental habitude of the specialist. That in-patient and out-patient services are best conducted under single control and with the members of the same staff functioning in both departments, and that it is contrary to the best interests of physicians, of patients, and of society, to establish hospitals for the exclusive benefit of either rich or poor, I firmly believe.

Teaching is not a function of the university hospital alone. Hospital staffs everywhere should cultivate the teaching habit, and their efforts to do so will be richly rewarded by public and professional recognition and by enhanced usefulness. It is with feelings of mingled admiration and pity that one contemplates a hospital which ministers successfully to its patients and to its patients alone — admiration for its beneficent work; pity for its failure to make its work count to the advantage of all of the sick of the locality, a result which can readily be won by encouraging physicians not identified with the staff to use the laboratory facilities of the hospital, to consult its library, to visit its wards, and to attend its clinical conferences.

The hospital which aims to reach the highest pinnacle of usefulness will conduct a school of nursing, but will not assign to its younger pupils tasks for which they are not yet fitted. It will be careful in the choice of those who instruct its pupils, and will pay them adequately. It will keep in mind the need of mental stimulation for instructors and supervisors, as well as for pupils. To overcome the tendency to mental stagnation, it will vary the tasks of its permanent staff from time to time, will provide a well-furnished library for their use, and will arrange lectures and demonstrations for their benefit. It will exclude from the school those who are not physically fitted for nursing work, and will guard the health of its

nurses by limiting the hours of their employment, by providing suitable dormitories, by furnishing plenty of wholesome food, by installing facilities for recreation, by establishing a system of periodic physical examinations, and by applying the most approved scientific means for the prevention of diseases to which nurses are exposed.

Throughout the hospital there must be respect for all its workers as well as tender regard for the sick; the spirit of service must be shared by all. Brilliant physicians cannot preserve the sanctity of a hospital which disregards the needs and rights of its most humble workers and thus deprives them of self-respect and of a sense of the usefulness and importance of their work. In the ideal hospital, the health of the workers will be deemed as precious as that of the patients; and, lest under the pressure of a multitude of tasks this essential duty be forgotten, let me urge each hospital to keep a record of the sickness occurring among its employees, so that the duty of maintaining among the working population of the hospital a sickness rate at least as favorable as that which prevails in the community at large, may never be forgotten. Let the hospital be a real health center for the members of its own organization.

A moot question among hygienists is just what constitutes an ideal unit for purposes of health administration. I am confident that a big city is not such a unit; for, although for the purpose of controlling environmental factors which are inimical to health, large-scale organization is necessary, the creation of health habits in the individual may be regarded as the foundation of public health, and in a great community the individual is beyond the effective reach of central authority. It has been said that the family is the ideal administrative health unit; the school is by some so regarded, the workshop by others. But the hospital is family, school, and workshop combined. Conceived in a spirit of service for the protection and promotion of health, possessed of every known resource for the attainment of its object, the hospital, whether public or private, sectarian or non-sectarian, while striving to render perfect service to its patients, should aim to become a model household, where health and happiness prevail.

HOOKWORM CONTROL AS A PROMOTER OF PUBLIC HEALTH AGENCIES

By

Victor G. Heiser, M.D.

INTRODUCTION

One hundred thousand persons die each year in the United States because they swallow some portion of the discharges of other people. One hundred thousand die each year in the Orient from beri-beri. Thousands upon thousands die annually in India from snake-bite. The deaths are only a part of the huge damage done, and for every person who dies there are from three to ten who are ill for days or weeks and often undergo some form of acute suffering.

Modern medical knowledge has long since discovered the means for controlling diseases due to the above causes, but administrative science or the art of application has not yet brought relief to a suffering world. It was largely with the hope that some contribution to the application of knowledge might be made that the International Health Board of the Rockefeller Foundation was organized. In order that a test might be made of methods that promised favorable results, a brief survey of existing administrative health methods was made. It became clear that all too frequently laws were enacted for which the public was not ready and for which it had not been educated. It is well to remember that for many years much of the world has been tending more and more toward democratic ideals and the dogmatic knowledge imposed from above is resisted by the people, sometimes by active but more frequently by a form of passive resistance and indifference. Sometimes a group of intelligent, public-spirited medical men and well-informed laymen have drafted legislation for the correction of obvious mistakes in public health methods. Legislators elected by popular vote generally fail to show interest in legislation of this kind, but by intensive propaganda and other methods legislators sometimes, as a personal favor to those immediately interested, have enacted the legislation.

PUBLIC HEALTH LEGISLATION AND EDUCATION IN THE SOUTH

Probably the first contact which the public had with laws of this kind was some form of prohibition, that is, a fine was threatened for failure to comply with health regulations. It was inevitable then that laws which came into existence under such circumstances seldom had popular support and consequently failed. If progress was to be made it was obvious that legislation should come upon the demand of the people rather than in spite of it. It was believed that if some single disease could be chosen which was widespread throughout the world and which lent itself to practical demonstration, the education of the public could be most easily accomplished. After considerable search it was decided that hookworm infection might serve the purpose of education. In order to test the idea, a million dollars was given to try the theory in the Southern States of America. When this matter was proposed to the Southern people it can be truthfully said that an idea seldom met with a more hostile reception, but by educational measures and patience, public opposition was overcome and when it began to be appreciated that real benefits to the individual could be secured by the application of hookworm measures, the public was inclined to listen more and more. Those connected with the treatment of hookworm disease in the Southern States were told to explain to the people among whom they worked that the same means that would prevent infection from hookworms would also be effective against the so-called intestinal-borne diseases. Typhoid fever, dysentery, cholera, and diarrhœa are conspicuous examples. Work was begun primarily among school children, but when the parents noticed how greatly their physical condition improved and when it became evident that in many instances their mentality also improved, intense interest was soon manifested. Very often the parents could be reached through the child. They began to ask for examination and were ready to take treatment if they were found to be infected with hookworms. Experience along these lines soon showed that if the individual can feel the benefit of a so-called public health measure in his own person, he soon shows an intelligent appreciation. It was by personal experience that a concept was formed in the minds of the Southern people of just what was meant when the term "public

health" was used. Frequently the question was asked of the doctors, "If you can stop typhoid fever and similar diseases, why don't you stop them?" The answer was obvious. Before measures against such diseases as typhoid fever can be taken, an organized public health department is necessary. Having seen the benefits following the treatment for hookworm diseases, a large part of the public was ready to venture further into the public health field and almost for the first time in the history of the United States popular demand arose for spending part of the revenues of the country for the creation of health services and the employment of competent health officers. When measures against hookworm disease were instituted, the entire Southern States were spending approximately $250,000 per annum for health work. In the last ten years public interest has increased to such an extent that now, upon the direct demand of the people, over $2,500,000 is being spent. In other words, public health in the Southern States is annually being safeguarded in a truly democratic manner.

THE INTERNATIONAL HEALTH BOARD

The success in America led to the creation of the International Health Board and the extension of similar methods to countries all over the world wherever opportunity offered. The International Health Board is now assisting in over thirty countries and governmental areas in the control of hookworm disease. Further control measures of this kind are applied for varying periods and it has followed in a large number of instances that a demand has arisen for the creation of better public health agencies.

The International Health Board of course undertakes many activities in addition to assisting in the control of hookworm disease. Frequently it happens that a scientific method for controlling a disease is available, but considerable experimenting may be necessary in order to arrive at an effective and economical administrative method. Preparations for health services throughout the world are felt to be too small to justify the spending of funds for purposes which do not produce definite results. Under these circumstances it often happens that the International Health Board may be of service in undertaking the experiments; and when an effective method

has been discovered, it can then be taken over by the official health agency.

The control of malarial fever is a conspicuous example. Since it was discovered that malaria was transferred by the mosquito, it has been obvious that if mosquito destruction could be brought about, malaria would cease. The world has not been able to avail itself to any great extent of this knowledge because the expense of methods of control has been greater than the communities could bear. With the hope of discovering simpler methods and practical demonstration procedures, the International Health Board began experimenting in conjunction with state and federal agencies, with the hope of providing something within the reach of the average Southern state or county. In this they were at least partially successful. It might now be said that in the majority of the communities in the Southern States malaria can be brought under control at an annual cost of a dollar per capita, and frequently with a maintenance cost of fifty cents per annum thereafter. Now that the method has been discovered, many communities are availing themselves of the knowledge and putting it into practical effect. In the tropics economical methods for the control of malaria in many areas are not yet available. With the hope of being able to contribute something toward the solution of this problem, experiments are now being undertaken in Porto Rico and Nicaragua and it is more than likely that other tropical countries will be added to the list.

It is frequently asked why something is not done toward attempting the application of health measures in China. Up to the present time it has not been possible to formulate a plan which offers reasonable hope of being permanently useful. If health measures are to succeed, there must be an official central health agency that is efficient. How to create it, is the present problem. The hope for the future lies largely in well-trained young Chinese doctors. Perhaps they may be able to fashion the wedge which will open the way toward a solution, and foreigners may be of some help in assisting to drive the wedge after it has once been started.

INTRODUCTION OF DR. WILLIAM H. WELCH

By

GENERAL LEONARD WOOD, M.D.

Dr. Houghton, Ladies, and Gentlemen:

I hope you will understand my rather overdecorated appearance; I have come here between the courses of an official dinner. I am delighted to be here and I have come with a very definite purpose. I want to invite your friendly attention to conditions of public health in the Philippine Islands. We are going to try to steal some of the funds of that wonderful combination known as the Rockefeller Foundation, which is doing a world-wide work of inestimable value to humanity — one of those splendid things which spring upon the world from time to time and do untold good.

We have many difficult problems in the Philippine Islands. We have a people who are generous-minded, willing, and anxious to improve. I think we can say without reservation that no other people under the friendly tutelage of another nation has accomplished as much in the space of twenty years as have the people of the Philippine Islands. We have led them through the bewildering mazes of government, and sometimes in our impatience we have forgotten the swamps through which our own people struggled to attain suitable government. In this respect the Filipinos are doing very well. But there is still a great field for work in public health. We have one great experiment which I hope we shall bring to a successful termination, that is the demonstration of the curability of leprosy. Dr. Heiser, who was responsible for the carrying on of this work in the old days, is going down again for a time. We have six thousand lepers assembled on one island, and I believe that we have the means of curing 50 or 60 per cent of them. We have a wonderful opportunity in the Philippines to demonstrate whether or not we have the cure of this terrible scourge, and when I take over my new duties there I am going to try to push this work forward. We have also an opportunity to do more and more work in Asiatic cholera. Indeed, I think that the medical work in the Far East is one of the most

important tasks that can be undertaken. It can be said truthfully that the average Filipino is born, lives, and dies without medical treatment or nursing. There are few doctors, great areas without a hospital, and very few dispensaries. There is a great opportunity to build up a splendid health service. We want to build up the School of Tropical Medicine, which formerly was one of the best in the Far East. We want to re-establish the Bureau of Science, which is doing very valuable work but has fallen upon evil days. And we want personnel. We want co-operation and interest.

I feel that the experiment in government in the Philippine Islands reaches not only every portion of the Islands but also all peoples who are struggling with self-government and who have ideals of a republican form of government. We are going to make this experiment a success.

I am here tonight primarily for the purpose of presenting to you a man whom you all know, an old friend of mine, a man who has done a great work for science, and through science for humanity; one of those men whose lives have been fruitful in great lessons, who have accomplished something for mankind, something which will endure as long as our race endures. I want to present to you Dr. William H. Welch of Baltimore, the father, — the dean, I should say, — of modern medicine, a man who has the respect of the medical profession all over the world and the love of all who know him.

THE ADVANCEMENT OF MEDICINE AND ITS CONTRIBUTION TO HUMAN WELFARE*

By

William H. Welch, M.D.

INTRODUCTION

Dr. Houghton, General Wood, Ladies, and Gentlemen:

I am sure I am expressing the sentiment in the mind of everyone present in telling General Wood how gratified we are that he is able to be here even for these few moments. It is not the first time that he has done me personally this great service, always with this very generous estimate of the little I have stood for and have been able to accomplish. General Wood's name is honored in every assemblage of medical men. Doubtless you know the part he played in that interesting story, told to us in so fascinating a way by Dr. Vincent the other evening. I have heard General Gorgas say that he doubted whether the Yellow Fever Commission, headed by Walter Reed, would have been able to accomplish the purpose for which it went to Cuba, had not General Wood been Governor at the time, because he so fully appreciated the significance of the results desired. You will recall that Reed's experiments were carried out upon human beings, fortunately without loss of life, and, with full knowledge of what he was doing, he assumed the responsibility for these experiments. At that day the lower animals were not known to be susceptible to yellow fever; and although Noguchi has since shown that it is possible to use them in experiments on yellow fever, nevertheless it is doubtful whether the discovery of the mode of transmission of the disease could have been made without its transference to human beings. Everything possible was done by General Wood to facilitate the work of Reed and his colleagues. It is pertinent to the theme I wish to speak about tonight to call attention to the great service which a man in authority at that time was able to render to a group of scientific men. We owe him a great debt, and his name is to be honored not only for his service in other fields, but also for his service to medical science.

* From stenographer's notes.

On this occasion — the formal opening of the buildings and hospital of the Peking Union Medical College — I wish to speak first of the great hopes which I have for the contributions of the college to medical education and knowledge and thereby to the prosperity of this great country.

The theme I have chosen for my remarks this evening — the advancement of medicine and its contribution to human welfare — is one which I selected deliberately when learning that it was desired that I should speak during these exercises, knowing that it would be impossible for me to treat the subject in any comprehensive way. It is a subject so broad and general in character, however, that I realized that it would enable me to talk upon almost any topic, for there is practically nothing in medicine that cannot be discussed under this heading.

It seems to me worth while on this occasion to consider to some extent what have been the circumstances which have tended to the advancement of medicine. Scientific men give, as a rule, very little thought, from a philosophic point of view, to the particular methods which they employ. A great philosopher, Francis Bacon, attempted to indicate how science was to be advanced. In his *Novum Organum* he set forth in great detail an elaborate system, which he conceived would, if applied, lead to the advancement of knowledge in every field of science. Of course it was a great contribution to human thought, and marks an era in the history of philosophy. But Bacon's work, important as it is from the side of philosophy, has never made quite the same appeal to investigators in science; the judgment of his own physician, whose name as an investigator is one of the greatest in the whole history of medicine, William Harvey, is that of many a man of science, namely, that Bacon talks about science as one might expect a Lord Chancellor and philosopher to talk. Bacon had no conception of what was really going on. Harvey and a great contemporary, William Gilbert — two great men of that period — together with Galileo and Keppler, introduced the era of experimental science. But little mention of the discoveries of these men is made by Bacon. This is an illustration of how nearly futile it is to attempt to indicate the precise methods by which science, natural or physical or medical, is to be advanced.

EARLY HISTORY OF SCIENCE

Nevertheless it is worth while to pause and look backward and draw lessons from the history of these sciences as to what in the past has contributed to their progress. Natural science, of course, is advanced by observation and by experiment, and the dividing line between the purely descriptive or observational period and the experimental period is rather sharp. These periods are fairly well defined by the year 1600, at which time the testing of theories, speculations, and hypotheses by experiment came to be recognized as of supreme value. Practically all medicine before that time was observational. Experiment is, of course, observational; it is observation under controlled conditions — conditions deliberately set up by the experiment. This period, then, introduced by the work of Harvey for medicine and by Galileo for physical science in general, brought a new era into the history of science.

I may say here in passing that it is worth while considering how far the mere observation of the phenomena of disease can bring us, and that it seems to me it is only fair to compare Chinese medicine with that observational period; that is, with Western medicine as it existed before the year 1600. We heard the other day at the Dedication Exercises from the Minister of Education that there were ancient Chinese students of disease. But their theories were resolved, one might say, into formulæ, and native Chinese medicine has never entered upon the period of experimental science, as Western medicine has done. I think it would be very interesting to make some comparison between the knowledge obtained in Western medicine by the mere observation of the phenomena of disease and the knowledge that has been secured by the Chinese observers.

THE BEGINNING OF RATIONAL MEDICINE

We usually begin our history of rational medicine with the name of Hippocrates. What existed before his time is more or less in the nature of folklore, and was largely priestly medicine. This has, indeed, never died out. It has always existed side by side with rational medicine. Though it has always been a thorn in the flesh to the regular doctor, this method for the cure of disease by influence over the mind — faith cure, or psychotherapy — is a perfectly legit-

imate method of cure and is to be studied in its effects. Rational medicine begins, then, with the name of Hippocrates, in the most brilliant period of ancient Greece, the Periclean Age. His name typifies the observation of disease unhampered, relatively at least, by speculations and theories, and stands so definitely for the direct line of approach to the study of the phenomena of disease that to this day we speak of the Hippocratic method, meaning a method of the objective study of the symptoms of disease as they present themselves at the bedside, with little aid from other sciences — anatomy or physiology — and little influenced by speculation or theory. It is not quite certain, however, that Hippocrates was so uninfluenced by speculation and theory as we are led to suppose. The writings which go under the name of the Hippocratic writings consist of the genuine writings and the false writings. The so-called pseudo-Hippocratic writings are eliminated from the genuine writings largely on the basis of whether or not they contain speculative doctrines. But since the discovery some years ago of the note-book of a contemporary student, whose comments, there is evidence to believe, are from the genuine Hippocratic teachings, and contain a great deal of speculation, I think that the conception that Hippocrates was uninfluenced by speculation and theory is not altogether well founded.

There have always been periods in the history of medicine when a wholesome cry has arisen, "Back to Hippocrates," meaning that those who have become entangled in speculation and theory, whose studies seem to be rather remote from the practical problems of disease, should turn back to the solid ground on which Hippocrates stood; to the straightforward, clear, unhampered observation of the phenomena of disease. His method stands today as important as it has always done. I do not propose to indicate here, even briefly, the progress which it was possible to make by that simple method of studying disease, but there are one or two points to which it may be worth while to call attention. Hippocrates was eminently sane in his views. He believed in natural causes for the origin of disease. It was a bold step forward when he made the statement concerning epilepsy, which was called the *morbus sacer*, that this disease was no more sacred than any other disease, meaning that it was due as

much to natural causes, mysterious as these might seem to be, as was any other disease; that all disease could be traced to natural causes. He had a conception as to certain essential points connected with epidemics. His work on airs and waters and places is the beginning of sanitation — it is a classic. His observations and his books on epidemics are valuable even to this day, and one can go back to those books and read descriptions of disease which have hardly been surpassed since. All this was accomplished by the clear observation of the phenomena of disease.

DOCTRINE OF CONTAGION

It is curious that most of the writers of classical antiquity had little or no conception of the conveyance of disease by contagion from person to person. One might think that such a conception would be very obvious, but as a matter of fact the doctrine of contagion plays very little part in the writings of Hippocrates and of his successors, even as late as Galen in the second century after Christ. Galen believed that the diseases which we now call the infectious diseases were spread very largely through air, through contaminated air, often emanating from vitiated surroundings, such as swamps. This very important conception of contagion originated long before the experimental era, and illustrates a point of importance, namely, the progress of medicine due to devastating epidemic diseases; for one may sometimes question whether the saving of human life from the careful study of great pestilences has not been larger than the loss of life by such scourges. The doctrine of contagion was brought forcibly to men's minds by the great epidemic of the Middle Ages, the "black death," which was probably the pneumonic plague. Then there were leprosy, smallpox, and typhus, and also syphilis, which made its appearance in Europe toward the end of the fifteenth century.

Very interesting views, therefore, as to the nature of contagion were reached without any experimentation at all but simply by study and analysis of the manifestations of contagious diseases. The work of Fracastorius on this subject appeared in the early part of the sixteenth century. He, by the way, was a humanist and a poet, and his name is of importance in the Renaissance, in the

revival of letters. His great work on contagion is amazing and almost modern in its inferences and arguments. One almost expects him to say, although he does not, that contagion is something alive. He says it is not of the nature of a poison, because it propagates itself among an indefinite number of persons and can spread from person to person. He speaks of the seeds of contagion and points out their characteristics; that they spread sometimes by direct contact, sometimes by very indirect contact, and sometimes by articles contaminated by persons and not directly from person to person.

MODERN ERA: THE STUDY OF ANATOMY

The modern scientific period in the history of medicine, although still purely observational, began with the dissection of the human body, with the study of anatomy. This period is often spoken of as the revived study of human anatomy, because there is evidence that human dissection was done far back in that ancient period about which we know so little, the Alexandrian period, from about the time of the death of Alexander, 322 B. C., on for three or four centuries — a very extraordinary period, the writings of which are lost. I should like to mention that what we know of this period is obtained largely from the writings of a non-medical man, Celsus, who is the only authority we have for the statement that vivisection upon human beings was done in the Alexandrian period. I have never felt that the statement of a lay writer such as Celsus, writing over two centuries later, should be accepted as conclusive, for vivisection upon the human body is not mentioned by Galen nor by any other of the medical writers who refer to the Alexandrian school. A positive statement, therefore, that human beings were vivisected for scientific purposes in the Alexandrian period is, to say the least, very doubtfully founded, although some medical historians do accept it.

The study of human anatomy was revived with great success by Vesalius in the middle of the sixteenth century. Its immediate significance was less for practical medicine than for the sharp break which it made with the acceptance of authority through tradition, which since the time of Galen had shackled the progress of medicine. From the middle of the sixteenth century human anatomy came to

occupy a very important place in medical education; and it was the only subject, until comparatively recent years — that is, until about one hundred years ago — with which the medical student came directly into intimate and personal contact. The rest was taught him by lectures and demonstrations. He learned only by being told about things, or reading about them. The study of anatomy had then, therefore, an educational value which it can hardly be expected to possess so exclusively today, although I do not for a moment mean to imply that it is not of the utmost value today.

The introduction of the modern era in medicine by dissection of the human body is worth dwelling upon for a moment in its relation to the situation in China today. When I was here in 1915 I attended a banquet to which many distinguished Chinese scholars had been invited to meet our commission. There was a great scholar present, the most distinguished, I was told, of the province of Hunan, one of the literati and a man greatly honored by the Chinese. After others had spoken there were cries from the Chinese in the audience for this man to speak. He made the following statement, which I have never forgotten: "While I have been sitting here I have been thinking, 'Why is it that Western medicine has so far outstripped Chinese medicine?' They started together, with the same object, the observation and cure of disease. One has gone ahead and the other has lagged behind. I think it is because we stopped dissecting the human body in the time of the Han dynasty." It is to a large extent the extraordinary ignorance and really fantastic ideas about the anatomy of the interior of the human body which have held native Chinese medicine enchained.

EXPERIMENTAL MEDICINE: PROGRESS IN PHYSIOLOGY

As I have said, there came into medicine the experimental method early in the seventeenth century. Medicine has usually kept pace with the great periods of advance in the natural and physical sciences. When these sciences are decadent, medicine is decadent or unprogressive. The great period of the seventeenth century, the period of Galileo, Keppler, and Newton in the physical sciences, of Bacon, Descartes, and Leibnitz in philosophy, and of Harvey,

Malpighi, and Sydenham in medicine, is comparable only with the nineteenth century in its awakening of human thought and in the rapid progress made in knowledge, and particularly in those branches of knowledge to which the experimental methods available at the time are applicable. There was great progress particularly in physiology. It is difficult even to conjecture what medicine would be without a knowledge of the circulation of the blood. The discovery of the circulation of the blood is, of course, one of the most brilliant achievements of the experimental method — an achievement obtained by experimentation upon animals, which doubtless could not have been obtained in any other way. And I may say here, in reply to the antivivisectionists, that the experimental method is as essential to the progress of medicine as it is to chemistry and to physics. It involves experimentation upon the lower animals, and it necessitates, of course, a high sense of responsibility in the carrying out of the experiment, which should be done always for a serious purpose and with every precaution to avoid the infliction of unnecessary pain. Fortunately today such experiments can be carried out under anesthesia without pain. We must not forget how fundamental is the debt we owe to vivisection. Even doctors themselves are rarely concerned with the origin of the knowledge they possess, and usually when we have to make statements to the general public, as in sessions of the legislature, or in a political campaign such as that recently in California, we cite concrete instances of the great benefits to and saving of human life from the experimental method, without pausing to think that without the results of experimentation we should not today be making intelligent observation of the pulse, or respiratory phenomena, or digestion, or the nervous system, or disturbances of external and internal secretions. We can now draw conclusions which would be quite impossible without the knowledge of physiology obtained from the purely experimental studies which the antivivisectionists are inclined especially to decry.

A great name of this century in medicine is that of Sydenham, who is often spoken of as the English Hippocrates, because, like Hippocrates, he gave little thought to allied sciences, even to anatomy and physiology, but confined his observations almost exclu-

sively to studies at the bedside. But it is not correct to say that the observational period is without its hypotheses and theories and speculations. Indeed those who most pride themselves upon being free from theories are often the most controlled by them. As an instance: until the seventeenth century the dominating theoretical doctrine of the origin and nature of disease was the so-called humoral doctrine, dating from the time of Hippocrates and Galen, the doctrine that disease was due to disturbances in the fluids, as contrasted with alterations in the solids of the body. This humoral doctrine was so inherent in men's minds that it controlled their practice. It was considered that there was a something, called "the matter of disease," the *materies morbi*, and that this must be eliminated from the body before persons could recover from their disease. Hence the use of cathartics, diuretics, venesection, and so forth. Here I may illustrate how progress is often made by purely empirical methods, often, one might say, by accident. A drug was introduced, the cinchona bark, which came from South America, introduced by the Jesuit Fathers from Spain, which cured malarial disease without question, and cured it without any critical discharge from the body. One can hardly conceive at this day why there should have been such a tremendous opposition to its introduction in the treatment of disease; but at that time its operation was simply incompatible with all the existing theories as to the nature of disease and methods of cure. Thus are men's minds often unconsciously tempered by theories and speculations.

As I have stated, there was at this period great progress in anatomy and physiology, and particularly in physiology. One great discovery I have already referred to, the circulation of the blood. Now there arose another conception, the importance of which is not so obvious, although it is well known to all physiologists. This relates to that important character of living matter known as irritability. No inanimate matter responds to external stimuli as does living matter. This action on the part of living matter was first noted by Glisson, though Haller in the eighteenth century is the one to whom credit is usually given. Still later came the discovery of the process and nature of combustion by oxidation and its analogy to respiration.

MODERN ERA IN PRACTICAL MEDICINE: PATHOLOGICAL ANATOMY

But practical medicine, real knowledge of disease, remained on an observational basis until the application of pathological anatomy; that is, until the recognition of the part which pathological anatomy can play in the elucidation of disease. This marks the beginning of the modern era in practical medicine, towards the end of the eighteenth century, with dissection of the human body in order to find out the seat and causes of disease. There had been in the sixteenth and seventeenth centuries postmortem examinations, with quite an accumulation of interesting facts relating to alterations produced in the human body by disease, but the conception that a true understanding of the nature of disease is greatly furthered by a systematic prosecution of postmortem examinations, was not really established in the minds of the medical profession until the publication of Morgagni's great work in 1761. (This work, I may say, appeared when he was seventy-nine years old, but the facts had been accumulated during his long life.) Now there came a great movement forward, a movement initiated by the study of the lesions produced by disease as revealed at the postmortem table. Fortunately soon after came the method of physical diagnosis by auscultation and percussion, and also the great discovery by Lavoisier of the part played by oxidation in respiration. Those three great discoveries were the stimulus for a movement forward previously unparalleled in medicine. The most glorious period in French medicine is, I think, the first two or three decades of the nineteenth century, characterized by the work of those men who with unusual ardor and zeal made such remarkable studies of disease by postmortem examinations, and also at the bedside and by auscultation and percussion. The great names of that period are Bichat, Laennec, and Louis.

INTRODUCTION OF THE LABORATORY

In that period came a great advance, the influence of which upon the progress of medicine it is hardly possible to overestimate. I refer to the introduction of the laboratory. There have doubtless always been workshops. It is difficult to imagine that Aristotle did not have something in the nature of a laboratory when one considers his

contributions in the field of natural history. But the laboratory as a place for teaching medicine and for research was introduced only in the third decade of the nineteenth century. It is usually stated that it came in with the establishment of Liebig's chemical laboratory in Giessen in 1825, but this laboratory was antedated by one year by the physiological laboratory in Breslau established by Purkinje. Liebig was greatly interested in problems of medical chemistry, in which field he was a great pioneer, as well as in the field of agricultural chemistry. The development of the laboratory is what gave German medicine its great prominence and prestige, for it was in Germany that its conception and development were advanced further than in any other country. I should be the last to decry laboratory teaching. It is of the utmost value and is the method by which the student is brought into immediate and direct contact with the object of study. But you cannot teach the whole content of any study in the laboratory; you must select, particularly in student courses, those aspects of a subject which are capable of treatment by laboratory methods. There is a certain lack of perspective in purely laboratory studies; they must be supplemented by reading, by carefully selected lectures on topics which are not included in the laboratory, and by recitations.

ETIOLOGY

With advancement in medicine came in the last quarter of the nineteenth century a great revolution, the penetration into the causes of disease. The era in which we are now living is characterized above all others by a recognition of the importance of understanding the causes of disease, and particularly the importance of an appreciation of and insight into the nature and causation of the infectious diseases. These which have always aroused the attention of mankind, on account of their devastating effects, have a social importance possessed by no other class of diseases, due of course to the fact that they affect such large numbers of persons at the same time and are often accompanied by so extremely high a mortality; and also the fact that they affect persons in the earlier periods of life — in infancy, childhood, and early adult life. Therefore the discovery of the causation and of the methods of prevention of this

class of diseases has a social, a racial significance which the discovery of the causation of the organic diseases of advancing life does not possess. Some of us doubtless would welcome an insight into the diseases of advancing life, if it were attended by methods of prevention and of cure. But the loss of persons who are reaching a period in which their activities are of less significance to society is not so deplorable as the loss of members of the younger generation.

SOCIAL ASPECTS OF MEDICINE

This line of advance, therefore, has really changed the face of modern medicine and given it a social and racial significance previously unknown. The discoveries in the field of the causation of infectious diseases have made laymen appreciate the importance of furthering the progress of medicine. And those are the diseases of greatest importance here in China. We who stand a little apart are filled with envy of those who are attacking this problem here, because you have a relatively unexplored field. I wish to pay tribute to all the work that has been done by the medical missionaries and others in the Orient; but they would be the first to concede that there are here open problems of the greatest importance for the saving of human life and the relief of human suffering.

These then are some of the things that have occurred to me to say, as influencing the progress of medicine. I should like to allude for a moment to the things that attract men to enter the field of science, and of medical science more particularly. I should like to refer to the rewards. And by rewards I do not mean merely financial rewards. I mean the satisfaction which comes from careers in these fields, the intellectual satisfaction, and the satisfaction derived from the respect and appreciation of one's fellow-members of the community. That kind of appreciation is very essential to the progress of science and of medicine. It is widely given in France and in Germany, with the result that a larger proportion of their best and ablest talent has been attracted to the field of science. I do not think the same can be said in equal measure of our country, America, where the rewards have been greater in other fields. Those who possess a distinct gift for advancing knowledge, a distinct gift for discovery, are comparatively rare, and therefore the larger the

number who are attracted to enter such careers, the greater the chances of there being among them this relatively small number possessing the capacity for fruitful investigation. This element of appreciation is, therefore, extremely important. It is, I think, something to be cultivated, and I believe it will come here in China.

I have not spoken about certain qualities in those who have been the great discoverers in medicine and who have contributed so largely to the progress of medical science. I think it is extremely important for young men to familiarize themselves with the lives of those who have devoted themselves so unselfishly and successfully to scientific discovery. Among such I would single out the lives of Harvey and Pasteur as particularly stimulating and inspiring to young men. Two excellent lives of Pasteur, one by Vallery-Radot and the other by Duclaux, have been translated into English. All that I have said tonight is exemplified by the life and example of such men as Pasteur.

Science has progressed in different ways in different countries. The great agency in France and Germany has been the university. In England the characteristic note has been independent investigation, a certain quality of independence, rather dissociated from organized effort in universities or societies, characterizing English progress. In America progress has been very largely associated with the development of medical education. At this point I should like to say that the success of independent institutes of research is dependent upon sound medical education. You cannot divorce research from university education. The supply of men who are to engage in such work must come from the universities. Notwithstanding the splendid results, fully justifying the establishment of independent institutions of research, it is true today that the great mass of contribution to knowledge comes from universities and medical schools. I believe the time will never come when capacity for the advancement of knowledge will not be regarded as an important qualification for the teacher in our best universities and medical schools, teaching and research thus going hand in hand. There will possibly be certain differentiations in the lines of work. Certain kinds of work, of great importance, can be undertaken best in independent institutions of research; and it may be worth while

considering to a greater extent than we do today what work is best undertaken in universities and medical schools, and what should be left to the independent institutions. The establishment of independent institutions of research in no way takes away from the importance of the scientific spirit and attitude of mind in the university and in the medical school, but rather should contribute to their development.

CONCLUSION

I have long overstepped the limits I had set for this address, but I wish in closing my remarks to express the thought that is in my own mind, and I believe in the minds of all who have had the good fortune to be present at the exercises of this interesting week, that it has been a week, in the first place, of the greatest enjoyment and pleasure, due largely to the hospitality which has been shown us on all sides, and that it has been also a week full of inspiration. It has brought those of us who have come from the West into personal contact with the problems and the situation here which I think is going to be of great importance to us, and which I hope will be of importance to you. We understand your problems better for having been here. We shall watch with the greatest interest and confident expectation the work which is done here. I have not dwelt this evening upon the purposes of this school, because they have already been set forth so ably and so fully in other addresses. But you may be sure, those of you who are workers here, and indeed in other places in China, that you are not lost sight of; that we shall eagerly follow your work and shall take a great interest in it; that you are as much a part of the world of medicine as though you were in your native countries. I also desire to express the confident hope that the purposes for which this school was established will be fully realized, and that it will serve as a beacon light and a center from which will radiate knowledge for the saving of human lives and for the welfare of this great country.

MORNING ADDRESSES

SALUTATORY

By

George E. de Schweinitz, M.D.

It is altogether fitting and proper that an expression of deep appreciation should be made, in which appreciation all my friends and colleagues from the Western world join, in that we are privileged to visit these beautiful buildings, erected on such broad and generous plans; to become acquainted with the work which has been done, an earnest of that which shall follow; to note the opportunities afforded to those who are banded together for the relief of human suffering and the prolongation of human life; and to observe the lines of research which are being established whereby that suffering shall be prevented, that life prolonged, which in other circumstances is too easily wrecked, too early cut short.

I perform a pleasant duty in conveying to the Trustees, Director, and Staff of the Peking Union Medical College from the Acting Provost and Trustees of the University of Pennsylvania, a message of congratulation and good-will. In like manner, representing the American Medical Association and fulfilling the directions of the Board of Trustees, I extend their salutations and best wishes, including in these greetings those of the large membership of that Association, and I bring with me, Mr. Director, formal credentials, duly signed and sealed, from the University of Pennsylvania and from the Trustees of the American Medical Association.

Happily for me, it has been my duty to share in the instruction of the young men of China who from time to time come to the School of Medicine of the University of Pennsylvania, and I desire to bear testimony to their outstanding mental capacity, their intelligence, their industry, and their insistent effort to succeed. To you, gentlemen of the Faculty of the Peking Union Medical College, I offer my felicitations in that your students are in largest measure recruited from the youth of this great country, who, entering this Temple of Medicine (and never before has this descriptive title seemed more appropriate), are offered opportunities of unsurpassed value whereby

they may acquire an education which shall enable them to extend far and wide the beneficent influence of the practice and art of medicine and of surgery and of the conservation of health. May great success attend you in all your endeavors. "Two things come not back," said the Caliph Omar, "the sped arrow and the spoken word." The arrow was found in the heart of an oak, but the spoken word in the heart of a friend. I leave with you these few inadequately spoken words in the full trust and belief that I leave them, too, in the hearts of many friends.

CONCERNING THE EVOLUTION OF SOME OF THE VISUAL PHENOMENA OF PITUITARY BODY DISORDERS

By

George E. de Schweinitz, M.D.

INTRODUCTION

This communication concerns itself solely with clinical observations on some of the visual interpretations of pituitary body disorders, as they have been noted in public and private practice, and as they have been studied in the service of Dr. Charles H. Frazier in the University of Pennsylvania Hospital, and in some instances, through his courtesy, in that of Dr. Harvey Cushing. There is no attempt to discuss the matter from the standpoint of literature-analysis, surgical procedures, or pathologic investigation. In its preparation, five previous papers on this subject have been utilized, and a number of the diagrams there employed are reproduced (1 to 5).

The term "pituitary body disorders," as employed, is descriptive of affections of the hypophysis in general, without, except in incidental mention, reference to the type, that is, whether there is excessive activity of the glandular epithelium (hyperpituitarism), or whether there is diminished function of the anterior lobe (hypopituitarism).

The important visual disturbances depend, for the most part, on compression of the optic chiasm, the optic tracts, and the optic nerves, in other words, of the basal visual pathways, and also, in a fair percentage of cases, on pressure on the motor nerves (10 to 25 per cent). They are the most common neighborhood signs of lesions in the hypophysis. Their relation to the size of the sella turcica is, however, not constant. Thus, in acromegaly there may be a very large sella without any evidence of disturbed visual function.

If in any case the effects of altered glandular activity should manifest themselves in outstanding features (gigantism, acromegaly, adiposity, and infantilism, etc.), recognition of the condition presents no difficulty; nor, indeed, are difficulties in this respect of moment, if visual field defects suggest the necessary general investigations, notably X-ray examination.

EARLY AMBLYOPIA

But the question arises, and has often been discussed, whether in the absence of these "outstanding features" ocular signs in association with certain constitutional symptoms may not lead to an early diagnosis and a correct interpretation. Many patients who are subjects of pituitary body disorders in an early stage (usually hypopituitarism), although entirely unaware of the nature of their disease, first consult an ophthalmologist, because headache, often of a "boring" character, some disturbance of vision, mental apathy, or somnolence, are the symptoms for which relief is desired, and which are believed to be due to eye-strain.

In these circumstances, however (at least, in some cases), the disturbances of sight cannot be corrected by glasses. It is a form of blurred vision of which the patient is definitely conscious, and which antedates the amblyopia, associated with nerve-head changes and visual field defects, especially scotomas, as ordinarily investigated. It may last for months (in one case for two years) before change in the color of the disc is notable.

Although twelve years ago, when first discussing this "prodromal amblyopia," or preferably "early amblyopia," I stated that a scotoma could not be demonstrated, there is reason to believe that working with modern methods a minute defect of this character, central or paracentral in position, could be found. As this amblyopia represents the earliest stage in the evolution of visual defects, its accurate investigation may well escape attention, just as its significance has often failed of recognition. The patient's visual acuteness (tested with a type card) at first may be normal, or standard, in the sense that the letters are correctly read at the proper distance, but not clearly, — read, as one patient said, "as if I were in a brown study." Evidently this amblyopia indicates the first result of beginning pressure or traction.

SCOTOMAS

The next step in the evolution is the formation of paracentral hemianopic scotomas; later "hemianopic (bitemporal) defects," and ultimately more or less complete bitemporal hemianopsia.

The small paracentral scotoma may develop into a larger bitem-

poral defect; it may remain small, and the temporal field loss may take place from the periphery, usually beginning up and out, until approximately the midline is reached, and the whole outer area of the field is dark.[1] Occasionally (three instances in my experience) coincidently with, or shortly after the appearance of the paracentral scotoma, a dark island appears in the area between the fixing point and the periphery, into which the darkening of the field from the outer margin merges.

A typical evolution would be as follows: (*a*) A visual blur not due to optical faults, possibly, but not certainly associated with a minute scotoma, of varying duration; (*b*) paracentral scotomas, either enlarging into extensive bitemporal defects, or remaining small, while the temporal visual field loss proceeds from the periphery; (*c*) quadrantic temporal hemianopsia; (*d*) complete, or practically complete, bitemporal hemianopsia (Figures 1 to 7).

A so-called typical development is by no means constant or uniform. In fact, referring now to the scotomas, they often are "atypical" in position and evolution, and for convenience may be classified thus:

1. Scotomas up and out from the fixation point; the larger scotoma being in the field of the eye with the poorer vision; later bitemporal hemianopsia (for example, Doyne's case (6)) (Figure 8).

2. Large temporal scotomas, either nearly symmetric in development (Pontoppidan, Uhthoff), or larger in one field than in the other, the enlargement of such defects associated with shrinking of the temporal fields from the periphery, resulting in total bitemporal hemianopsia. It is probable that an early stage of these large bitemporal defects consists in the appearance of the smaller paracentral (temporal) scotomas before referred to (Figures 9 and 10).

3. Binasal hemianopic scotomas, with, as in Zentmayer's case, a bitemporal color defect; they may be of short duration, in the case quoted, only two weeks (Figure 11).

4. Central scotomas: those which may simulate the scotomas of

[1] Very occasionally the first quadrantic defect is down and out, because the primary pressure has been on the dorsal fibers of the crossed bundle which supply the upper nasal quadrant layers of the retina. Cushing suggests that the lesion is of infundibular rather than of hypophyseal origin in these circumstances.

toxic amblyopia; those which are large and directly central; those which are primary in the sense of a first manifestation, and those which are secondary in that they may appear, as in Lauber's case, during a relapse of sight-disturbance, after a period of release from visual defects which may have been typical. Central scotomas are not common, but a number are on record (Nettleship, Lauber, Kocher, Bartels, Fleischer, A. Knapp, de Schweinitz, O. Hirsch, and other reporters) (Figure 12).

5. Scotomas in other positions: up and out in one field, and directly over the fixation point, capping it, in the other field, as in a case of Holloway's and mine; unilateral, small and temporally paracentral in one field and temporal color defect in the other field; or of the usual paracentral position and shape on one side and small and directly central on the other (Figure 13).

Pressure foci in the chiasm are usually made responsible for most of these scotomas. Thus, the bitemporal hemianopic scotomas may be due to circumscribed involvement of the crossed fibers of the macular bundle in the ventral portion of the chiasm; the quadrantic temporal hemianopsia which so often follows may be related to an implication of the crossed ventral peripheral fibers. It is possible that a symmetrically extending lesion on both sides of the posterior upper surface of the chiasm might affect the uncrossed fibers of the papillomacular bundle and produce binasal hemianopic scotomas. Even though a central scotoma, suggesting axial involvement, may have been the cause of visual disturbances, clear explanation of its presence may not be demonstrable at autopsy, as Bartels points out (7); but local toxemia is certainly an etiologic factor.

An explanation by J. Herbert Fisher of the genesis of relative scotomas of the macular bundle is that the process is the result of traction upon, rather than of pressure against, the chiasm, and that these macular fibers, owing to their highly specialized function, suffer more than the others. Cushing believes that the two conditions, pressure and traction, go hand in hand (8).

Another important factor in the development of visual field defects as the result of basal disease is vascular constriction. This was described and commented upon long ago. In 1852, Türck reported a case of carcinoma posterior to the chiasm which pushed this struc-

ture into an upward and anterior position; both optic nerves were found transversely notched by pressure of the anterior cerebral arteries. The notching of the optic nerves in patients with hypophyseal disease has been described by Sachs, the pressure coming from the anterior cerebral arteries, by Holloway and myself[2] and also by Siegrist. Such notching, or grooving, is not confined to the optic nerve; the optic tracts may be similarly affected by pressure of the anterior cerebral artery (Uhthoff, Bartels, Erdheim), and the chiasm by the anterior communicating artery (O. Hirsch[3]) (Figures 14 and 15).

Because special emphasis has been placed on the development of scotomas in pituitary body disease, it must not be supposed that such visual field defects are a new discovery. They have been known and commented upon from time to time for many years. Foerster (10) referred to a number of cases of "medial hemianopsia," as he was wont to call this type of visual field defect, which began with small negative scotomas in each field, lying close to the outer side of the fixation point, and which gradually increased in size until the whole temporal field was involved. That pituitary body affections may be etiologically active in this respect Foerster showed in that he quoted the case of D. E. Müller (11), observed more than fifty years ago, in which autopsy revealed that the chiasm disease which produced the visual field defect was caused by pressure of a tumor of the hypophysis.

Twenty-five years ago, Nettleship (12), basing his paper on an analysis of ten cases in which failure of vision at or near the center of the field in both eyes, with no early ophthalmoscopic changes, discussed central amblyopia as an early symptom in tumor of the chiasm. While three of them certainly depended upon tobacco intoxication, and one in all probability on the effect of alcohol, in the

[2] Some of the literature in this respect has been briefly analyzed by Holloway and myself (2).

[3] Recently Oskar Hirsch (9) in a review of the ocular symptoms in fifty-nine cases of tumor of the hypophysis submitted to operation (forty-five without acromegaly and fourteen with acromegaly), emphasizes the fact that the lesions of the visual paths do not depend alone, as is usually maintained, upon the pressure of the growth of the chiasm, or upon the stretching of this structure, but upon its strangulation as the result of vascular constriction.

others there was no reason to suspect a toxic cause. Three of the patients died with symptoms of cerebral disease, and in one a post-mortem examination revealed flattening of the brain on both sides, and at the cerebral base a membranous sac filled with fluid lying on the sella turcica and extending forward to the cribriform plate of the ethmoid. The wall of the cyst was loosely attached to the hinder part of the frontal lobe, to the median part of the tempero-sphenoidal lobe, and to the hook of the uncinate convolution. The chiasm was incorporated in the front wall of the cyst. In short, as J. Herbert Fisher puts it, Nettleship's series of cases emphasizes the necessity which exists for every ophthalmic surgeon to be familiar with diseases of the pituitary body, especially as these scotomas may in a later stage develop into typical examples of bitemporal hemianopsia, i.e. the field defects which are usually described as characteristic.

In Uhthoff's (13) statistical material concerned with hypophysis and infundibular tumors without acromegaly, among 148 ocular defects only three "central scotomas" are noted; among those with acromegaly with 180 records of eye-symptoms; "central scotomas" are classified as "very seldom;" paracentral scotomas are not listed; Bartels in a total of twenty-two cases of hypophysis tumor records approximately only three instances of central scotoma. A. de Kleijn (14), although he carefully describes the variations of the visual field in pituitary body disease, fails to note the presence of scotomas. Cushing (15), in his well-known monograph, makes no reference to scotomas, but in his study with Clifford Walker of chiasmal lesions with special reference to bitemporal hemianopsia (8), they are carefully noted and explained, with the statement that the presence of these scotomas was first "described in detail" by Bartels, in Germany, and by myself and Holloway in this country (2). They have been, however, particularly discussed by S. E. Henschen (16), by H. M. Traquair (17), by Bruno Fleischer (18), and by other authors whose reports are scattered through recent literature.

DEVELOPMENT OF TEMPORAL HEMIANOPSIA

Reference has been made in the discussion of the presence of scotomas to the shrinking of the visual field from the temporal periphery, and the gradual development of hemianopsia. Frequently

this begins with a "slanting off" of the field for white of the upper temporal quadrant (temporal slant, J. Herbert Fisher (19)), and may be, and usually is, associated with a quadrantic defect of the color field; rarely is the condition equal in degree, that is, symmetric in each field. As the result of the study of their material, Cushing and Walker have divided the period from the beginning of an advancing process to complete blindness into eight stages (8).

Briefly, slightly modifying the description of these authors, the typical progress is as follows: (1) Temporal slant of field for white; upper, outer quadrantic color defect; relative or absolute paracentral scotoma; (2) upper temporal quadrantic defect for white; increase in temporal color defect; paracentral scotoma; (3) complete color hemianopsia; increasing temporal defect for white which encroaches on the area below the horizontal line; paracentral scotoma; peripheral contraction beginning in preserved field; (4) complete hemianopsia for white and colors, sometimes with preservation of the macula; increasing density of scotoma; (5) increasing contraction of the remaining field on nasal side; absolute scotoma; (6) shrinking of the contracting preserved nasal field from the vertical meridian; greatly defective or completely lost color vision; (7) only remaining field a small area on the nasal side; (8) blindness (Figure 16).

The visual field alterations, just briefly described, do not, of course, represent observations in an individual case. As Cushing and Walker state (8): "These steps, or stages, have been selected out of the many possible ones for the reason that the larger number of our cases happen to have been caught in them, and not with the idea that the advancing process tends to halt at these separate stages." With this schematic series one may compare a series of charts from an individual case in my own practice, from the stage of temporal slant and paracentral scotoma to the development of complete hemianopsia (complete blindness did not occur), and gradually the return of vision and visual field function to complete restoration of sight and practically normal visual field extent. While the similarity is not exact, there is a notable correspondence (Figures 17 to 25).

It is well known, as Cushing and Walker emphasize (8), that the

process, to use their language, "rarely advances with equal steps in the two eyes." Thus there may be an upper quadrantic defect, or a complete hemianopsia in one field and total darkness of the opposite field — a not uncommon finding; or, in advanced cases, a small sensitive area may be found in one field, the other being totally dark, which is rather sharply defined, and which can be detected only with the aid of a small point of electric light; or the difference in the extent and character of the two fields may be much less exaggerated (Figures 26 to 28).

In Traquair's (17) brilliant essay, devoted to the study of bitemporal hemiopia (later stages) and the special features of the scotoma, and to an examination of the mechanism of production of the field defects, the conclusion is reached that in a normal or typical course of development of temporal hemiopia, the defect begins in the upper-outer quadrant, and gradually "the field is involved in a circular manner, the loss proceeding clockwise in the right field and counter-clockwise in the left, so that the upper nasal quadrant remains longest." In this respect the author does not agree with the Cushing-Walker scheme, where the last survival of function is placed in the lower nasal quadrant. Traquair believes the central defect or scotoma develops in the same way. Rönne holds similar views in this respect.

COLOR FIELDS

It is usually stated that the defect for colors precedes that for white and for form, and therefore it is proper that the color fields — blue, red, and green — should be carefully investigated; often the first color affected is green. The size of the test-object must be stated, because the defect (hemianopic or quadrantic) may be undetectable with a large-sized disc, but discoverable with a small disc. Accurate perimetric work cannot be done with an ordinary automatic registering perimeter; the Bjerrum method, the campimeter, Duane's tangent screen and small object perimetry must be utilized. With these methods and these cautions, early defects can in most instances be detected in the field for white and the uncertainties and difficulties of color perimetry can be avoided (Figures 7 and 9).

THE DIVIDING LINE

Although it is often asserted that in typical bitemporal hemianopsia the boundary line is vertical, in point of fact, in so far as the hemianopsia of pituitary body disease is concerned, this line is hardly ever regular or vertical. Doubtless a typical vertical meridian which bisects the macula does occur, but if so, the opportunity of finding it in these circumstances is uncommon.

INSTABILITY OF THE FIELD BOUNDARIES

A matter of some importance which has been dwelt upon by all observers who have carefully studied this subject, but notably insisted upon by A. de Kleijn (14), is the variations which the visual fields in some cases of pituitary body disease undergo. If daily or even more frequent perimetric examinations are made, a classical hemianopsia may be present at one time, but later it will be found that it has given place to an ordinary concentric contraction. Or the reverse is true; there may be a concentric contraction, due, doubtless, to pressure upon the peripheral optic-nerve fibers, which may even go on to temporary practical total loss of vision, and when the visual field reappears, a bitemporal hemianopsia can be demonstrated. De Kleijn refers to the so-called insular-shaped fields in hypophysis disease, these islands being subject to variations, not only in their number but also in relation to the part of the visual field which they occupy. These peculiarities in the perimetric examination doubtless depend upon the varying degrees of pressure of vascular and cystic growths in this region.

Because of this instability or fluctuating character of visual fields in certain types of hypophysis disorders, an incautious observer may be led into error in that he accepts "an enlargement of the visual field" as an index of improvement of the pituitary body condition, although it may well be that alterations in the size and shape of the field are temporary and in no way interpret a lasting relief of pressure.

HOMONYMOUS HEMIANOPSIA

Thus far the discussion has confined itself to scotomas, usually paracentral and bitemporal, and with partial or complete bitemporal (heteronymous) hemianopsia. While it is true that fully devel-

oped heteronymous bitemporal hemianopsia represents a visual disturbance which is regarded as typical and characteristic of affections of the hypophysis, it is far from true that this form of distortion of the field of vision is necessarily present as an ocular interpretation of pituitary body disorder. Referring to complete bitemporal hemianopsia, Cushing (15) writes: "Here, apparently, in many cases the condition lingers, and to this may possibly be attributed the fact that it has so long been regarded as the typical stage of the process."

Moreover, although homonymous hemianopsia due to pressure upon, or lesion of, an optic tract is less common than bitemporal hemianopsia in these circumstances, it is not true, as has been maintained, that it is "very rare" in hypophysis lesion. In common with other observers, I have studied a number of cases with this visual field defect, and Cushing has shown that these homonymous defects (among which, however, he includes "tendencies in this direction") are nearly half as frequent as bitemporal ones. This is an important point, because if not dwelt upon, or well understood, the presence of a homonymous defect in the visual field might turn attention away from the hypophyseal region, when in point of fact, it ought to be focused there[4] (Figures 29 to 32).

RESTORATION OF THE VISUAL FIELDS

As already pointed out, it is uncommon that the two eyes are affected to an equal degree, and therefore the visual field distortions are rarely even approximately symmetric. Should relief from pressure follow operation, or cure or improvement take place as the result of organotherapy or radium treatment, or occur, as very occasionally happens, because of spontaneous decompression, the restoration of the visual field limits usually develops from below

[4] Writing in 1906, Bartels (7) says that a so-called typical hemianopsia occurs in only about one-third of the cases of tumor of the hypophysis where the diagnosis has been confirmed by autopsy. Until the frequency of scotomas as a visual field defect in pituitary body disorders was recognized, their presence has, in many instances, led the examining physician astray in his diagnosis (20). Hirsch (9) records in his statistical material 7 per cent of homonymous hemianopsia. Evidently, if the growth proceeds backwards along the infundibulum, this form of hemianopsia would be likely to develop. Among approximately fifty clinical observations, I have found this defect (homonymous hemianopsia) in fully 5 per cent of the cases.

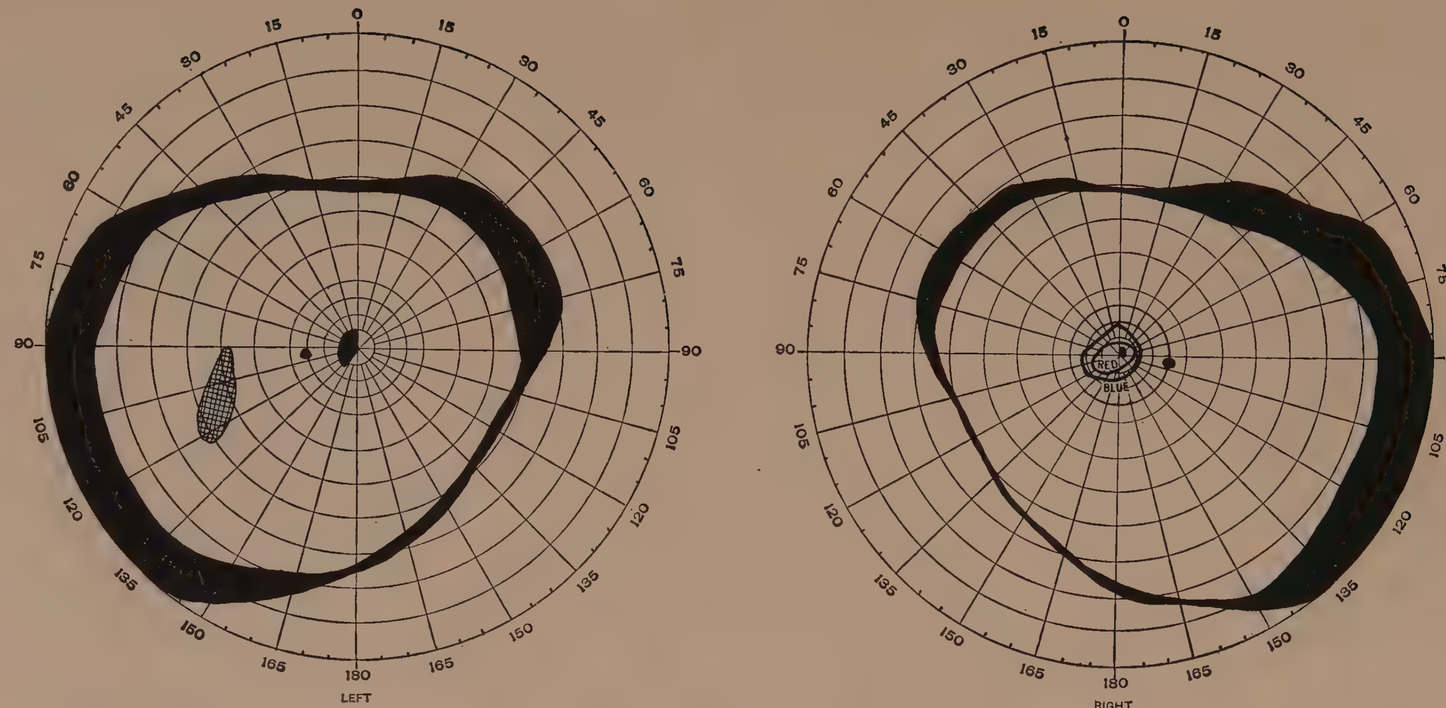


Figure 1. Pituitary body struma (probably). Patient ultimately cured by organotherapy. Early amblyopia (visual blur) lasted for seven months before paracentral scotomas were demonstrable. Right, tendency to color hemianopsia, small paracentral scotoma; left, large hemianopic paracentral scotoma, with slight concentric contraction and relative scotoma in temporal field midway between periphery and vertical meridian. Plotted May 20, 1910

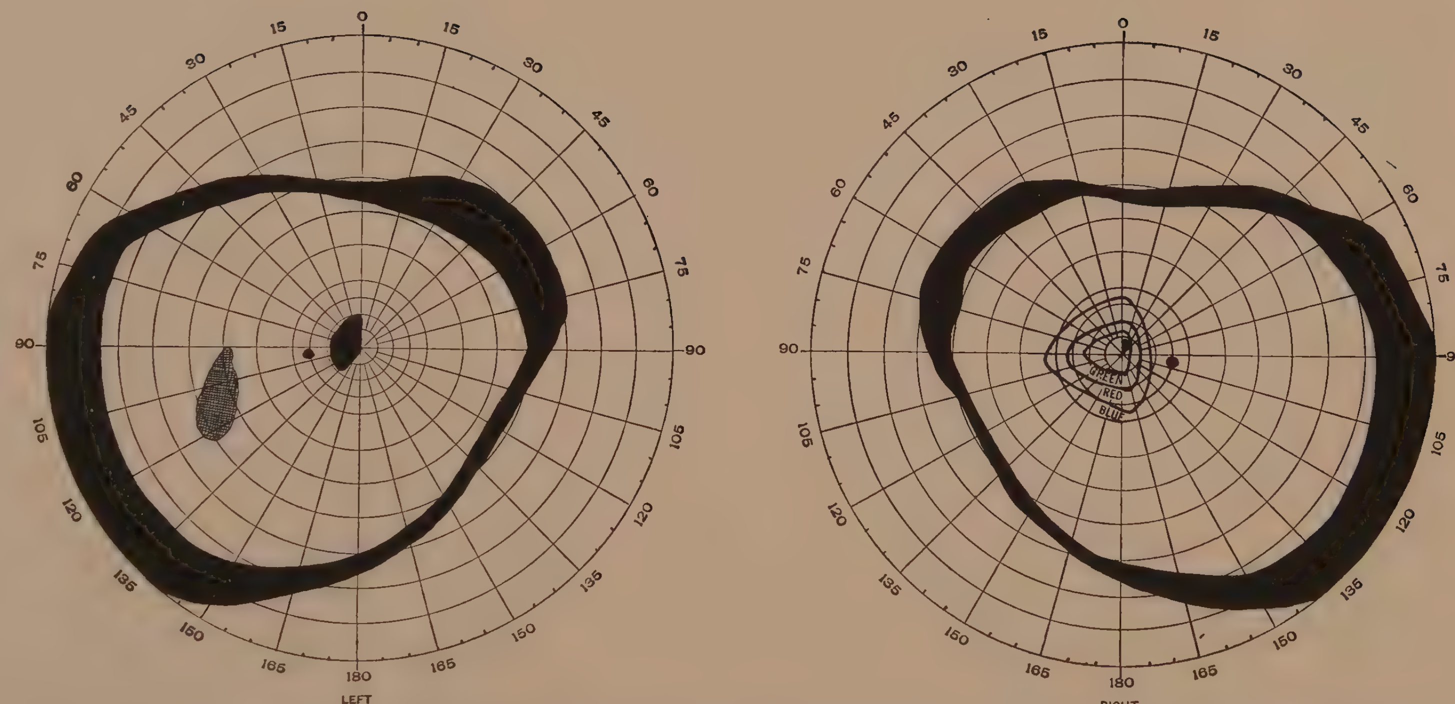


Figure 2. Fields of same patient as those depicted in Figure 1, plotted one day later; increase in size of left paracentral hemianopic scotoma and in density of aberrant scotoma; right, marked tendency to temporal color hemianopsia

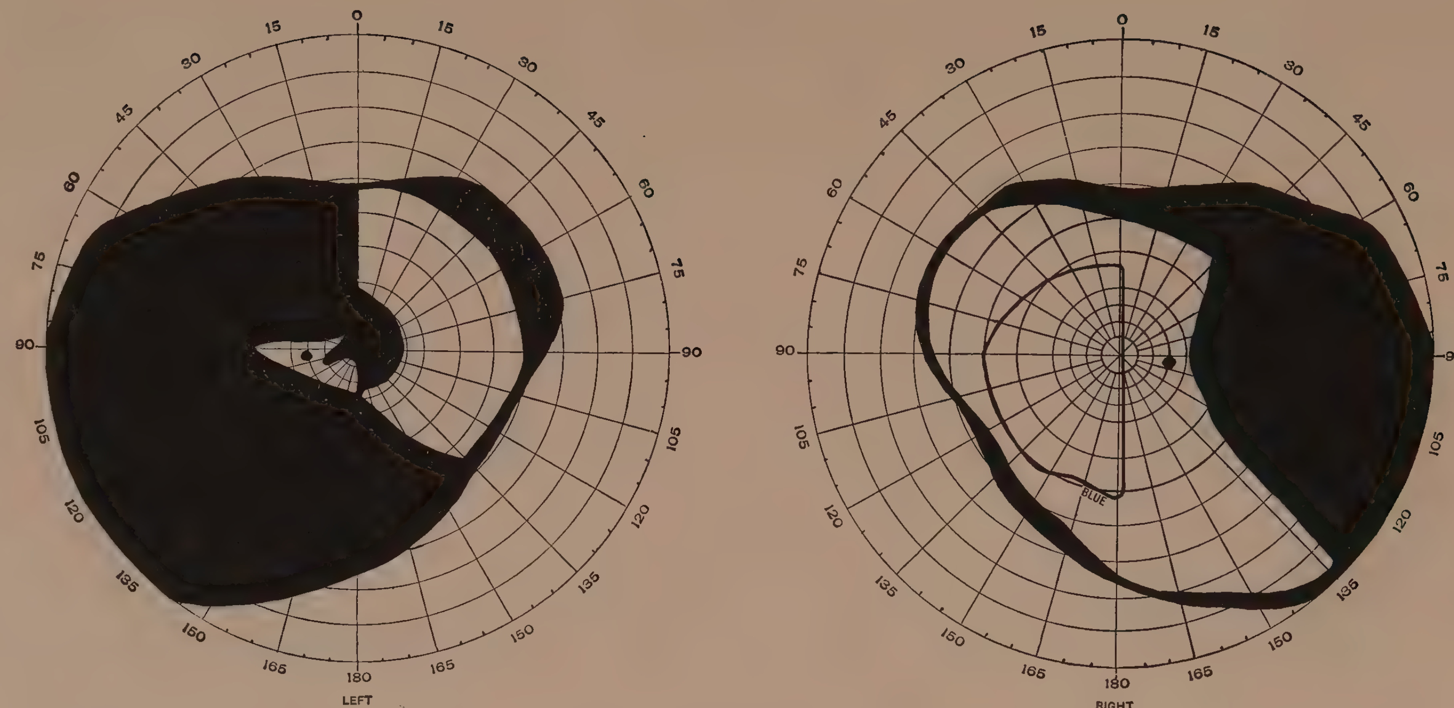


Figure 3. Fields of same patient as those depicted in Figure 1, plotted May 27; rapid deterioration; right, complete color temporal hemianopsia and rapidly advancing temporal hemianopsia for white, red, and green sense lost, hemianopsia for blue; left complete hemianopsia for white, except small patch of preserved field around blind spot; nasal field shrinking from fixating spot which is now obliterated by increase in size of scotoma, all color sense lost

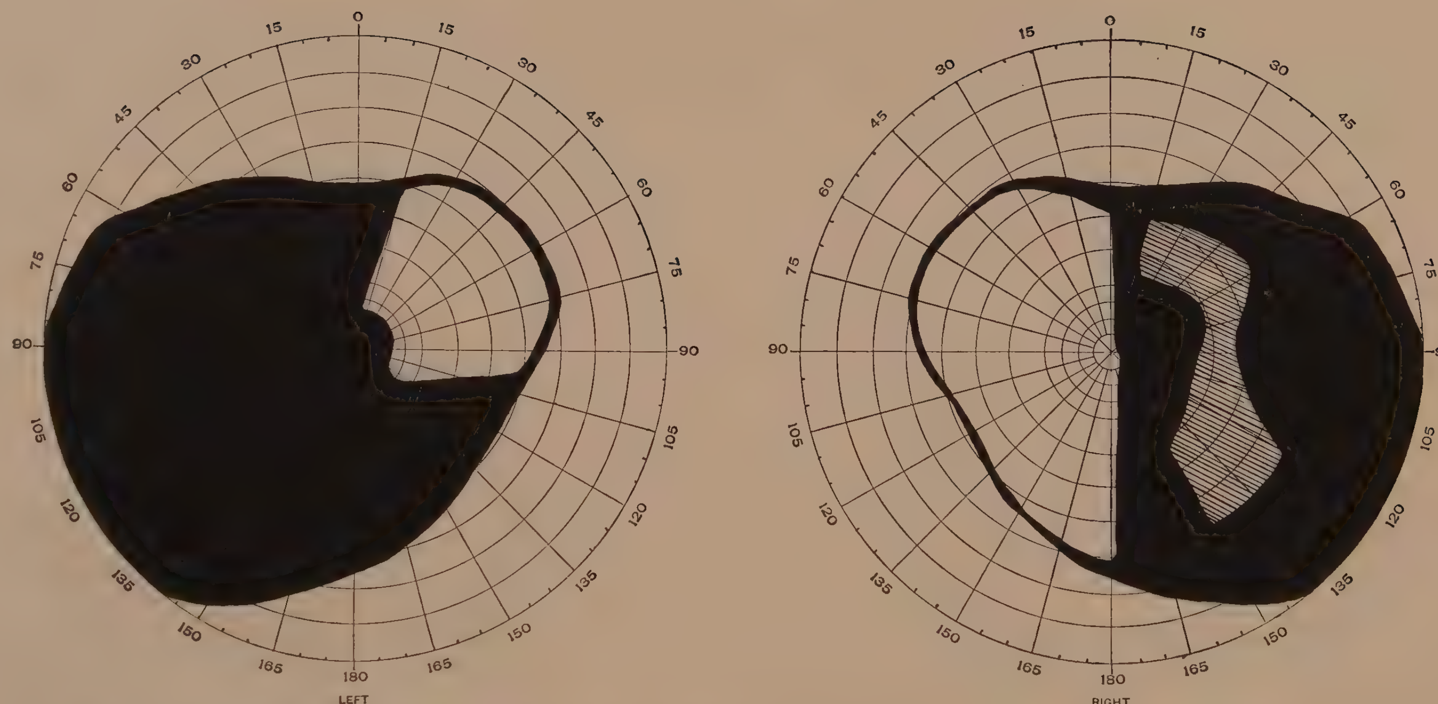


Figure 4. Fields of same patient as those depicted in Figures 1, 2, 3, plotted four days after field shown in Figure 3. All color sense lost; complete left temporal hemianopsia and shrinking of nasal field; complete right temporal hemianopsia, except an irregular island of faint light perception; one week later both eyes completely blind. Blindness lasted for twelve days in right eye and six weeks in left; ultimately restoration of vision and fields of vision under influence of organotherapy and mercury

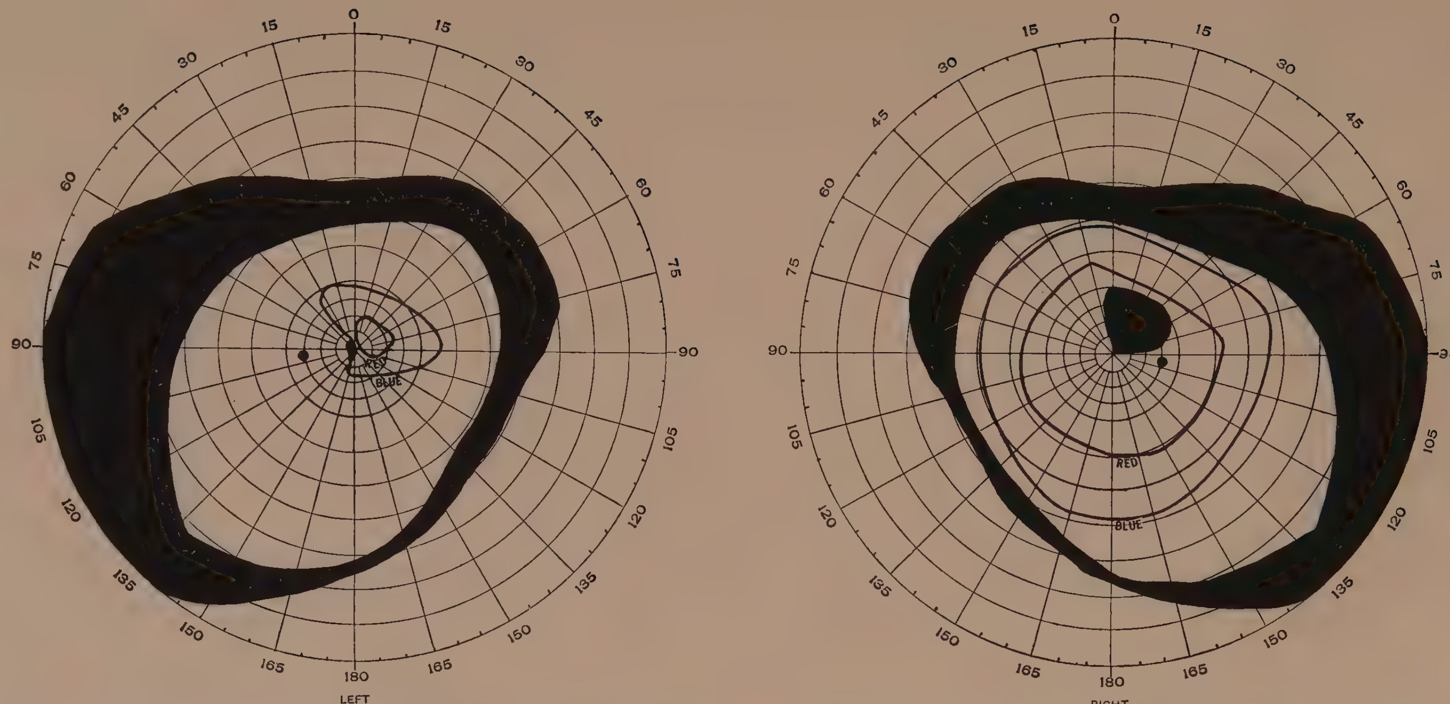


Figure 5. Fields of same patient as those depicted in Figures 1, 2, 3, 4. Right field (white) being restored from below. Left field being restored; irregular blue hemianopsia; complete for red; large scotoma, right, and small scotoma, left, persist

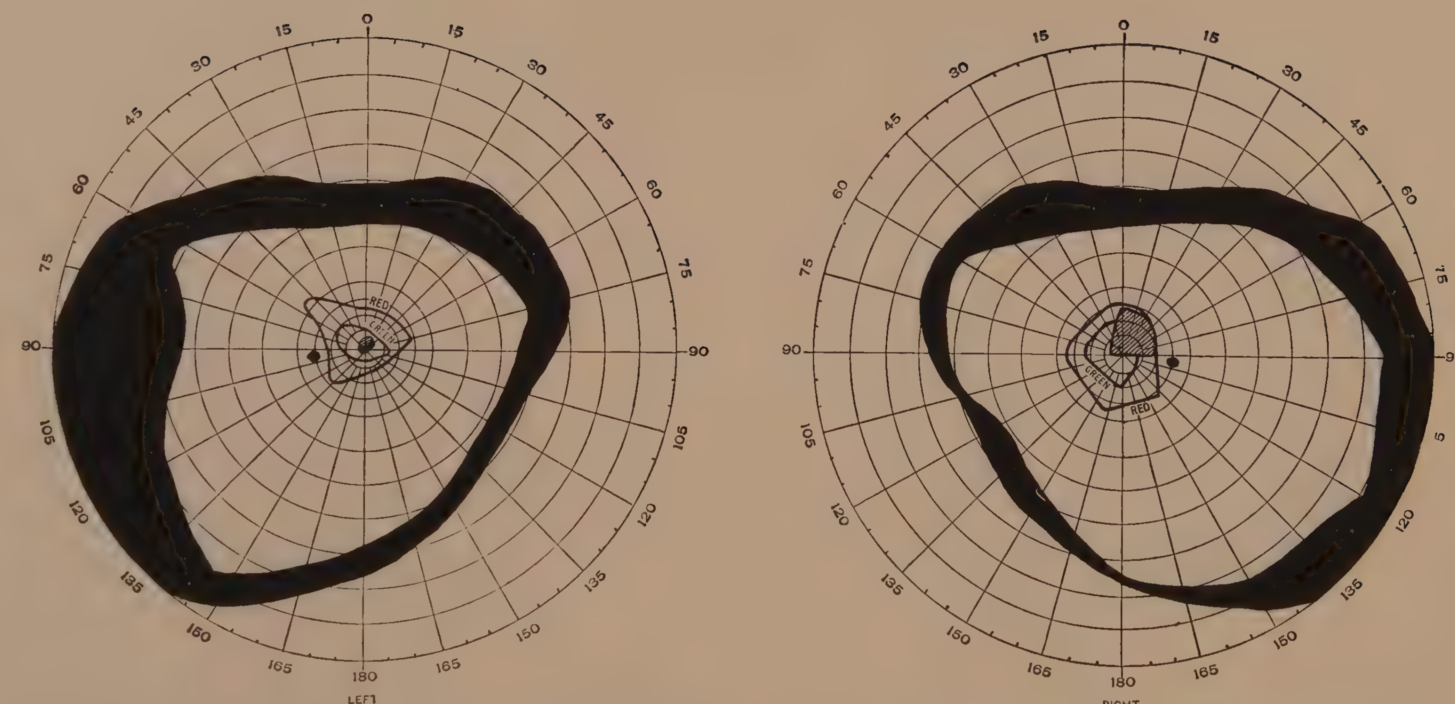


Figure 6. Fields of same patient as those depicted in Figures 1, 2, 3, 4, 5, after improvement began under influence of organotherapy. Note that scotomas, now relative, still linger; ultimately, as noted in legend Figure 4, cure was complete

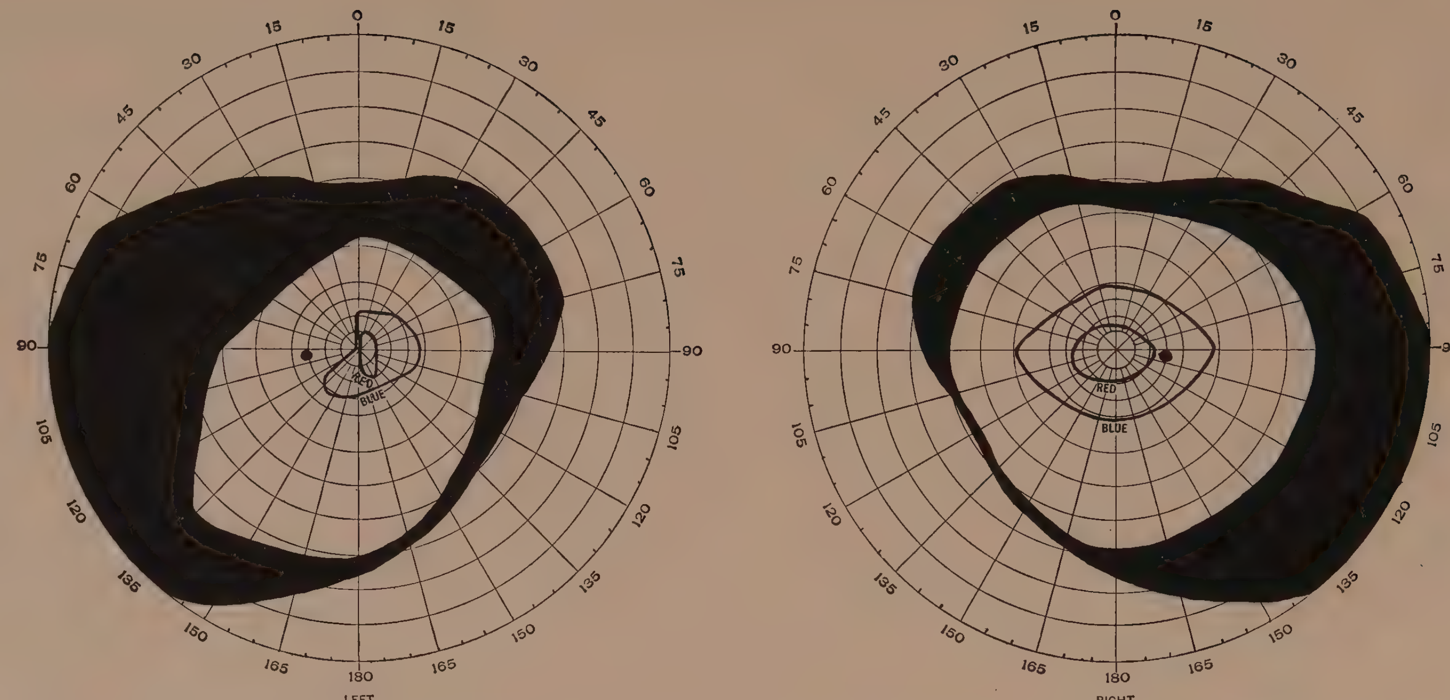


Figure 7. Field of same patient as Figures 1, 2, 3, 4. Scotomas no longer present; left quadrantic defect for blue; hemianopsia for red. Ultimate complete recovery

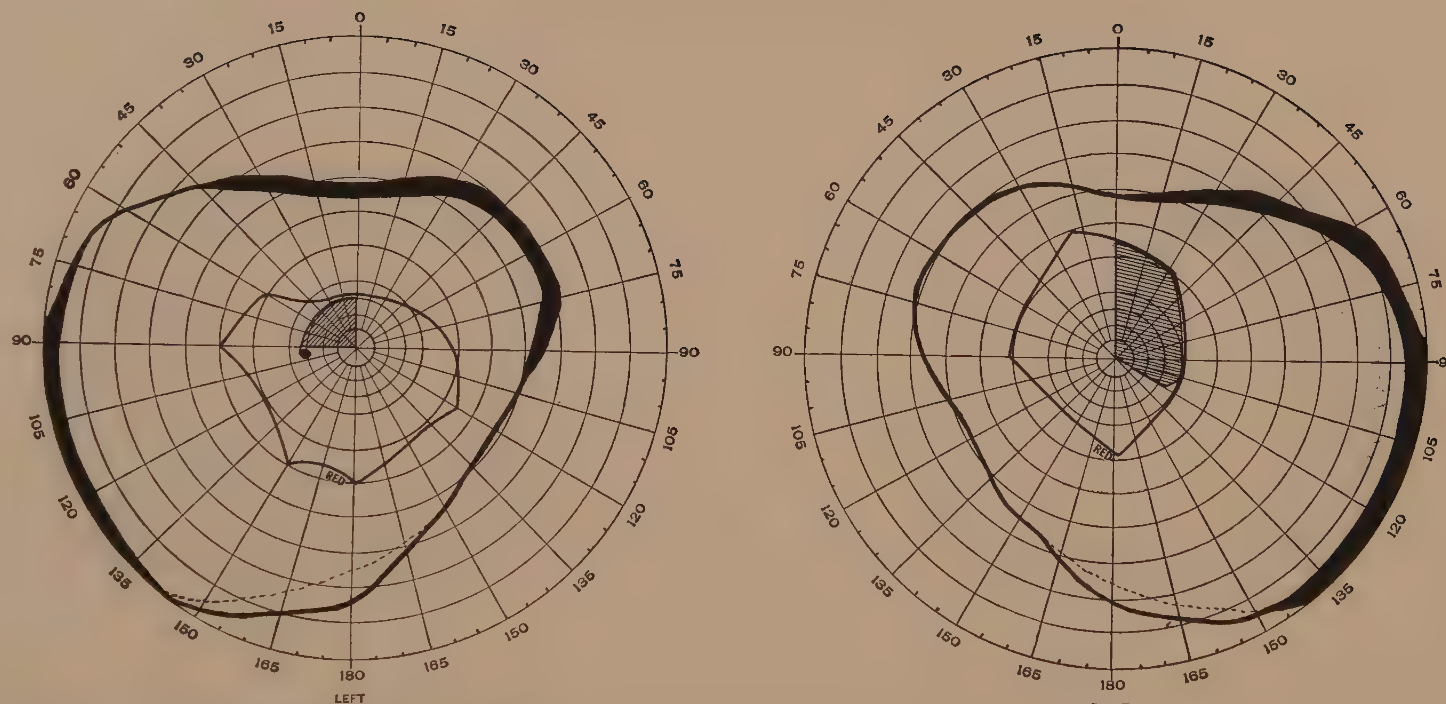


Figure 8. Acromegaly. Paracentral scotomas up and out, larger in right field; later bitemporal hemianopsia (Doyne's case)

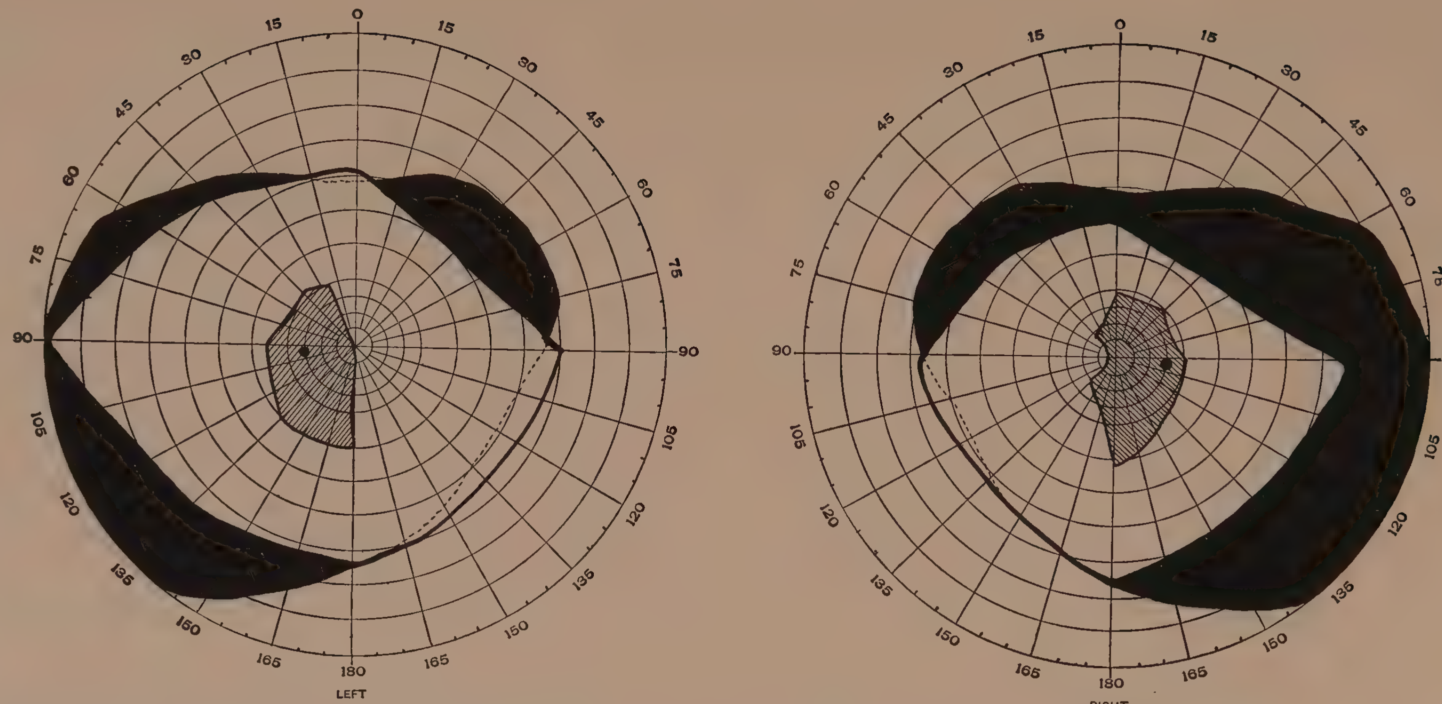


Figure 9. Acromegaly. Large bitemporal defects, with contraction of fields, and in left field a temporal slant (Pontoppidan's case)

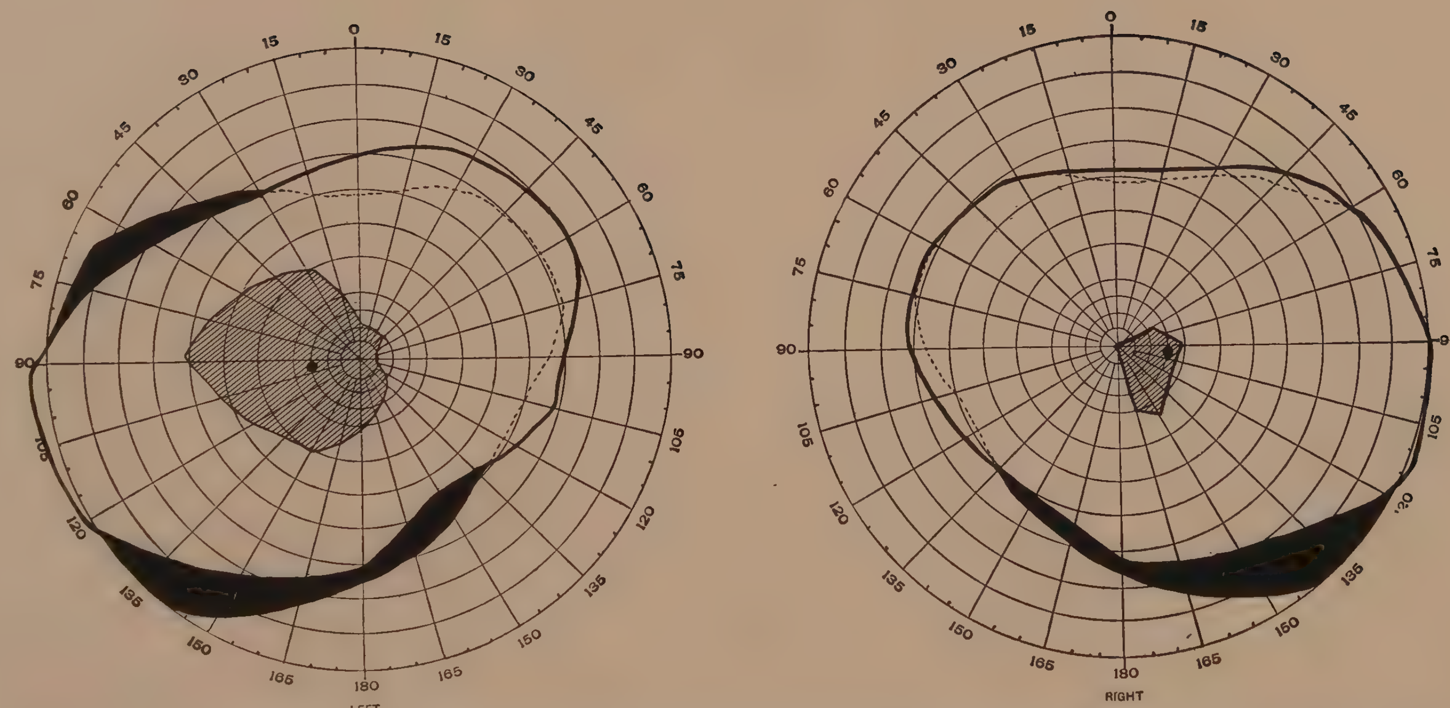


Figure 10. Acromegaly. Scotomatous defects, very large, and including fixating spot and proceeding temporalward in left field; smaller and paracentral, down and out, in right field; peripheral field practically unaffected (Marlow's case)

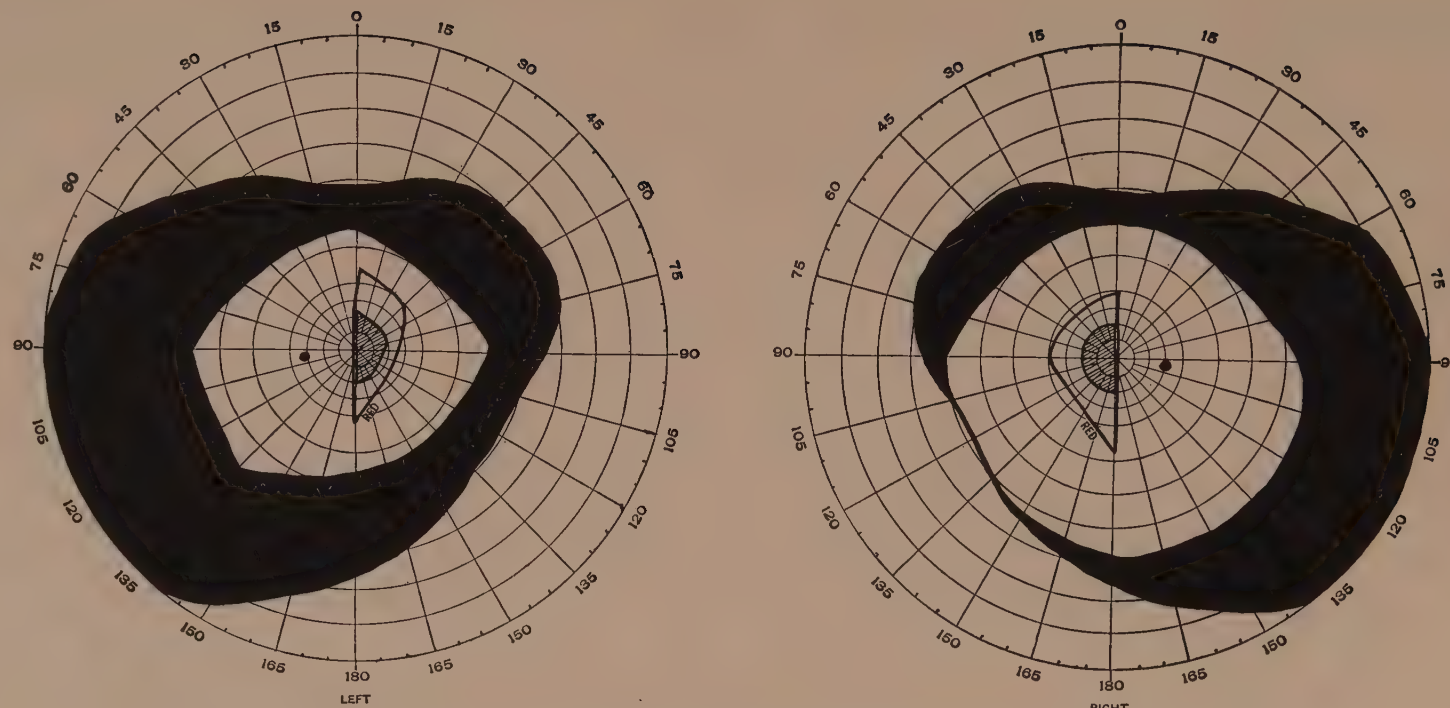


Figure 11. Acromegaly. Binasal hemianopic scotomas; bitemporal color hemianopsia (Zentmayer's case)

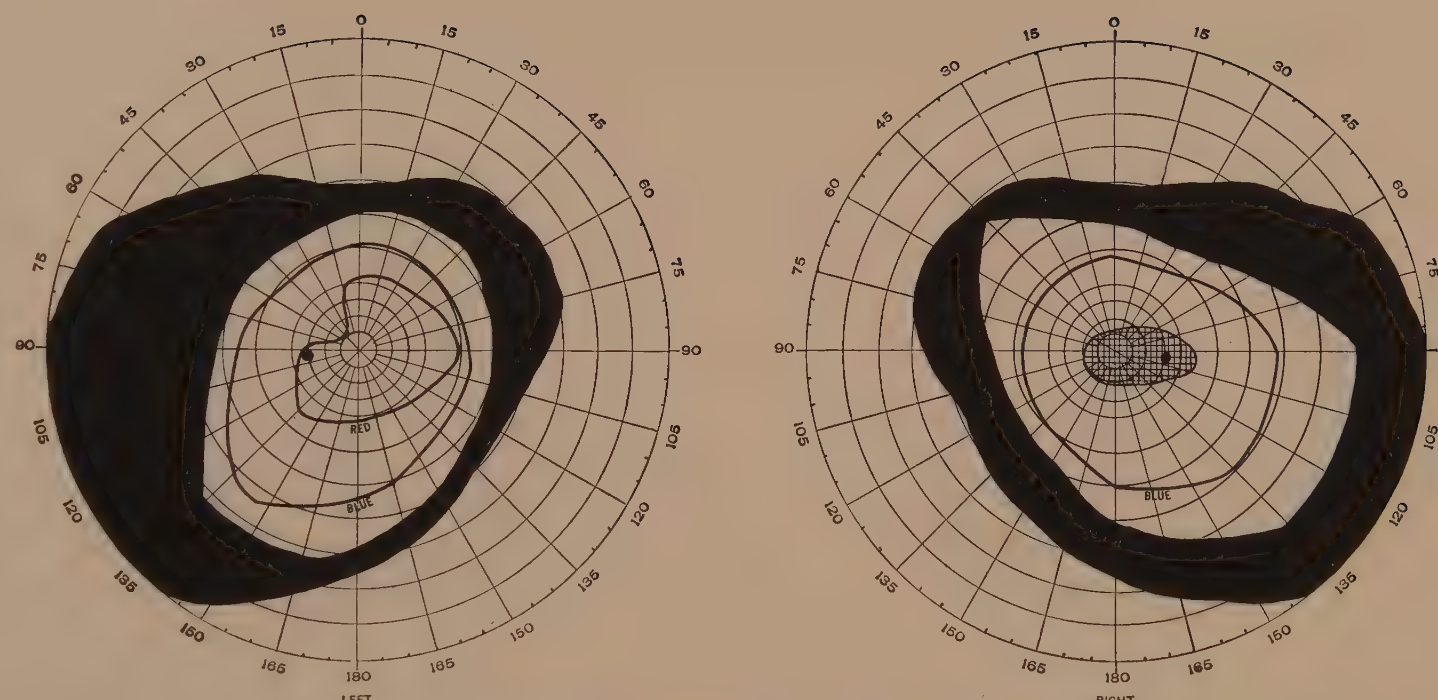


Figure 12. Pituitary body growth; defective vision noted, rather suddenly, after a long period of uncontrolled headache. Right, marked temporal slant in white field, loss of red and green sense, central relative scotoma; left marked slanting and loss of temporal field for white, quadrantic (up and out) defect for red; on campimeter screen loss of temporal red field was complete

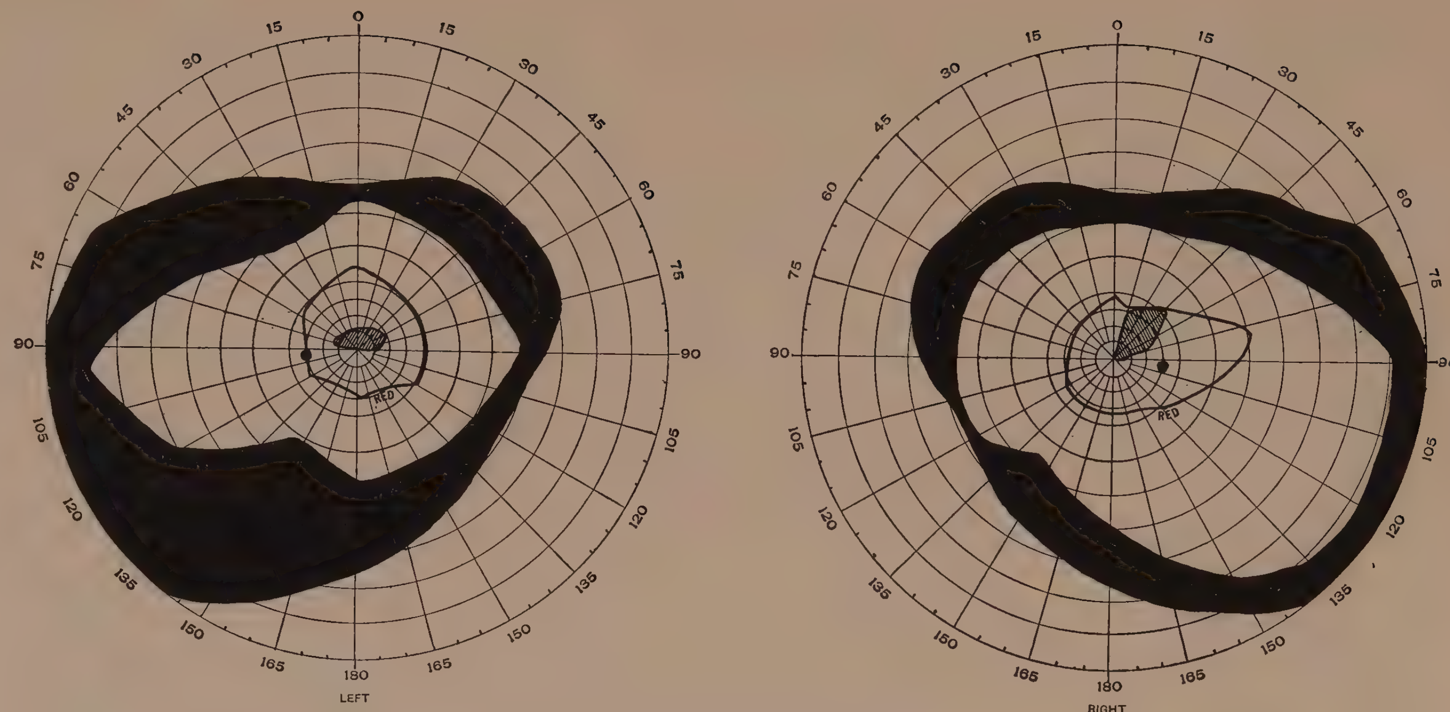
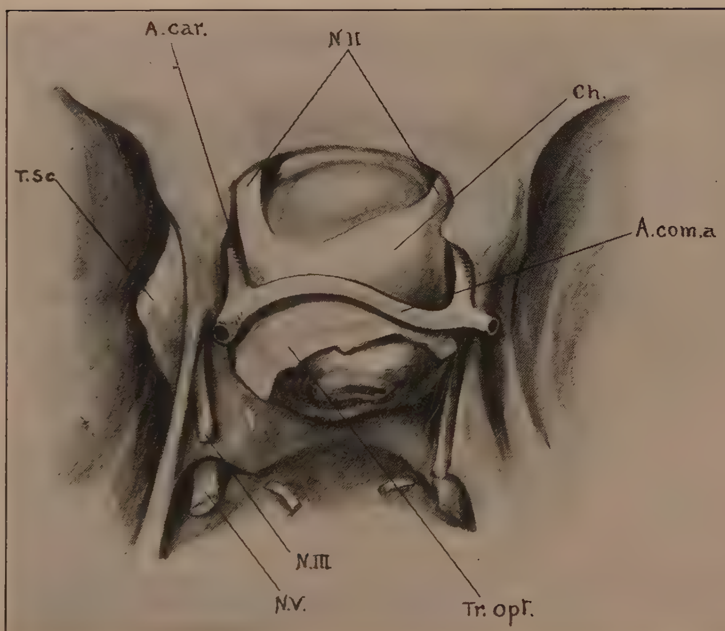


Figure 13. Acromegaly; paracentral scotomas, above fixating point, left field; up and out (usual position) right field



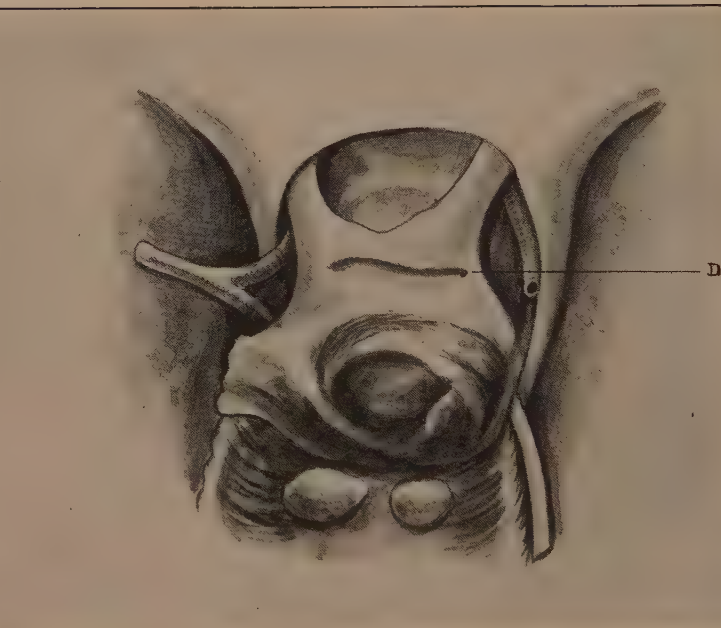


Figure 14. Showing pressure on the chiasm by a constricting vessel. *T.Sc.* tumor in sinus cavernosus; *A.car.* carotid artery; *Ch.* chiasm; *N II* optic nerves; *A.com.a* anterior communicating artery; *Tr. opt.* optic tract.

Figure 15. *D.* transverse groove in chiasm produced by pressure of the anterior communicating artery (which is turned aside). Diagrams after Oskar Hirsch (*Ztschr. f. Augenh.*, 1921, xlv, 308)

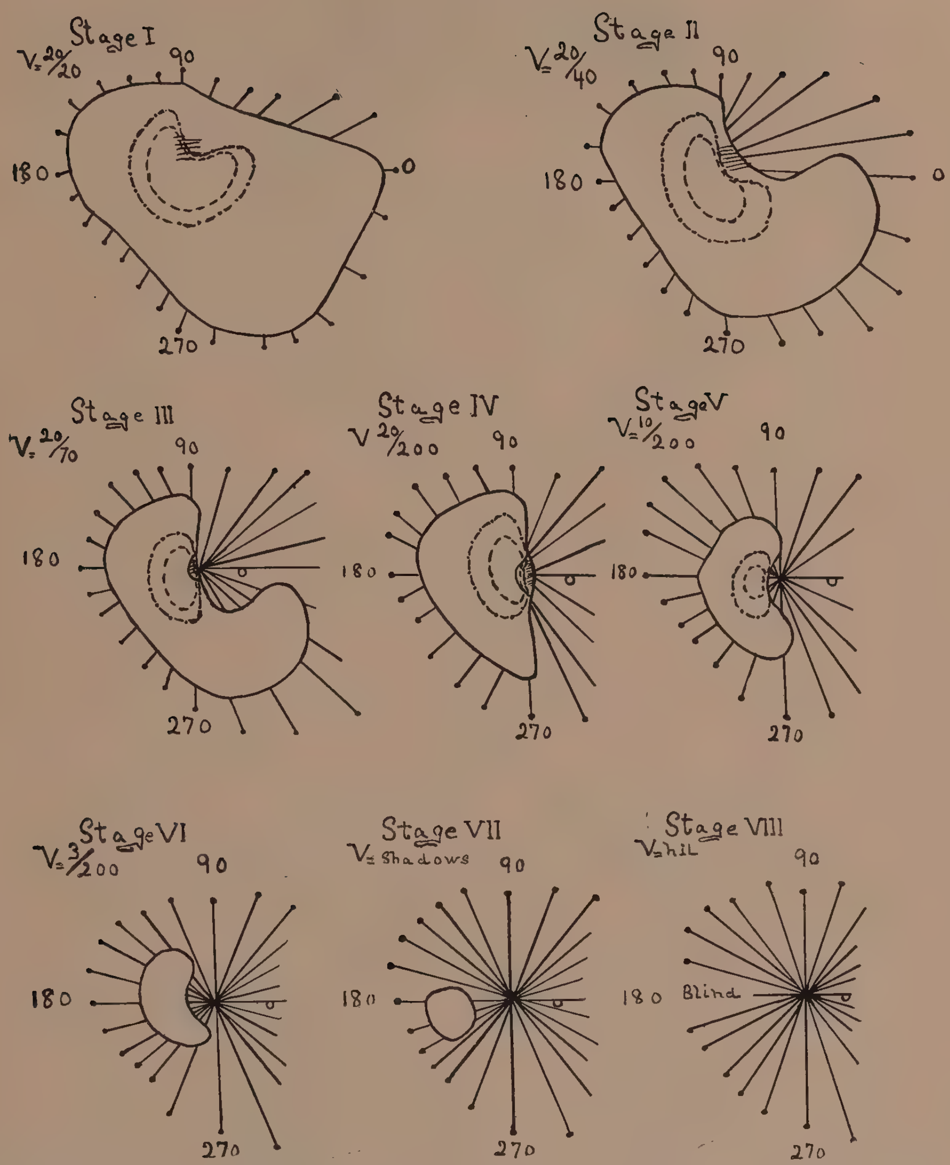


Figure 16. Eight stages of a progressing right temporal defect, according to Cushing and Walker

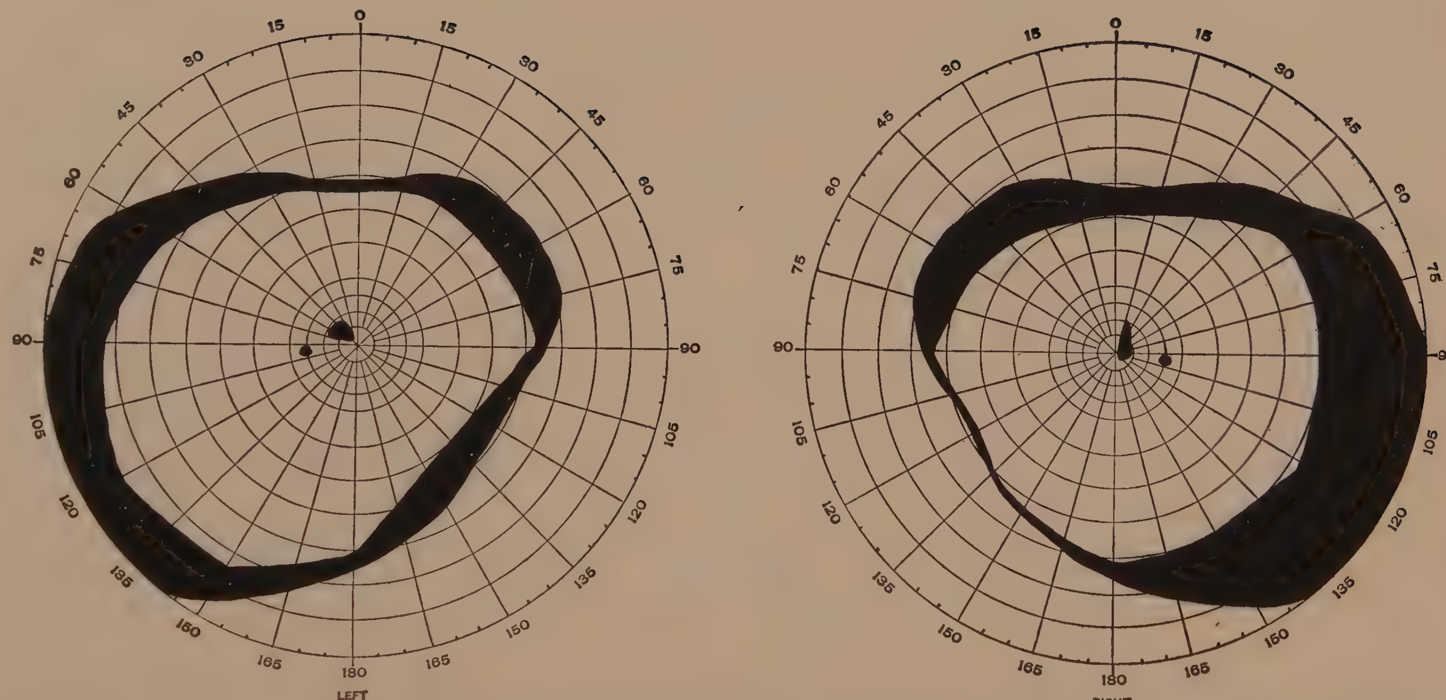
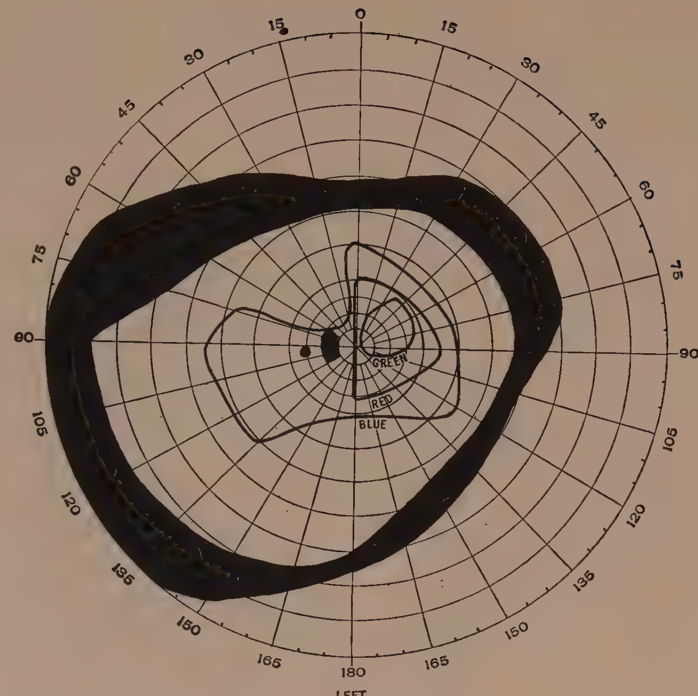


Figure 17. Pituitary body disorder, probably struma. Fields plotted a few days after decided visual blur was noted which had been preceded by a period of visual disturbance and headache. Paracentral scotomas up and out. O.D. V = $\frac{6}{60}$; O.S. V = $\frac{6}{10}$



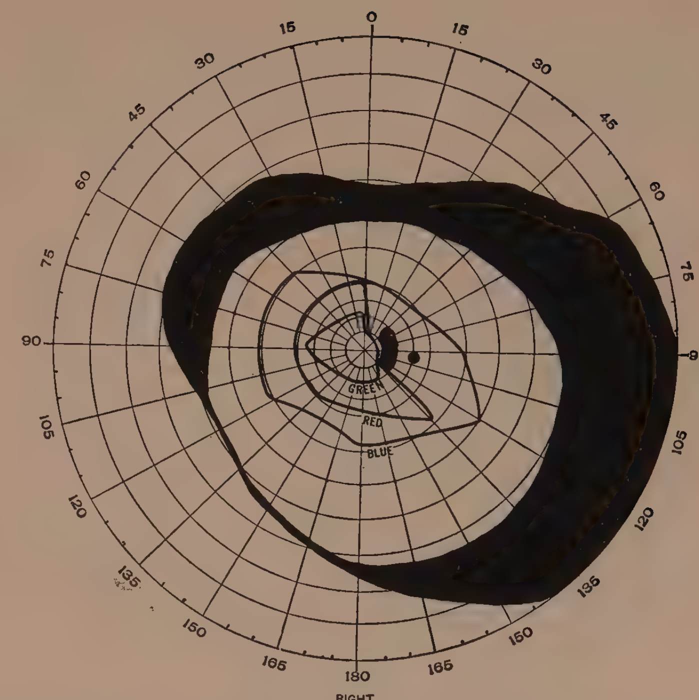


Figure 18. Fields of same patient as Figure 17, five weeks later; increased size and density of scotomas; right temporal slant (blue), quadrantic defect (red); practically complete temporal hemianopsia (green); left temporal slant (white); quadrantic temporal defect for blue, complete temporal hemianopsia for red and green. O.D. $V=\frac{6}{60}$; O.S. $V=\frac{6}{12}$. Glandular feeding begun

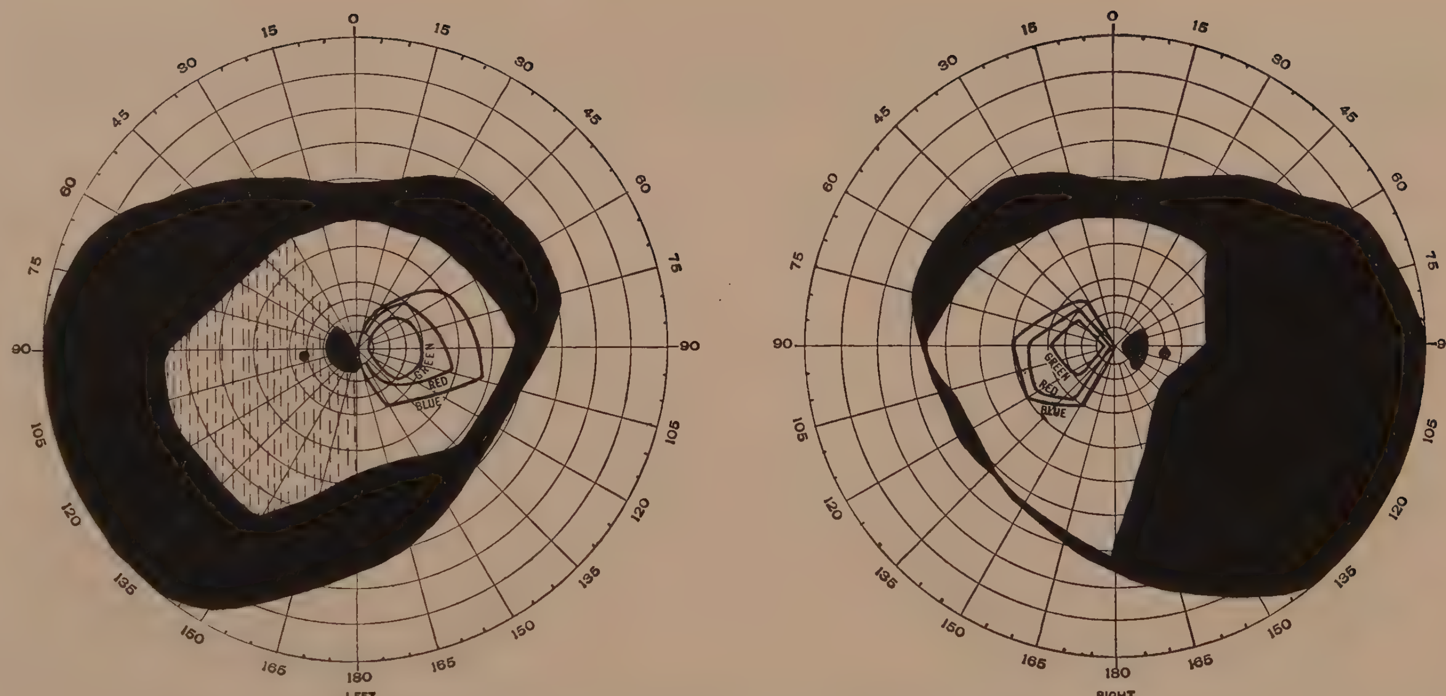


Figure 19. Fields of same patient as Figure 18, two months later; paracentral scotomas larger, but macula free in right field and not quite obliterated in left field; complete color (temporal) hemianopsia and almost complete for white, more produced below in right field; left complete color (temporal) hemianopsia, marked shrinking of white field, with area between encroaching dark field, and paracentral scotoma of faint light perception, anticipating complete hemianopsia, O.D. $V = \frac{6}{9}$; O.S. $V = \frac{6}{30}$

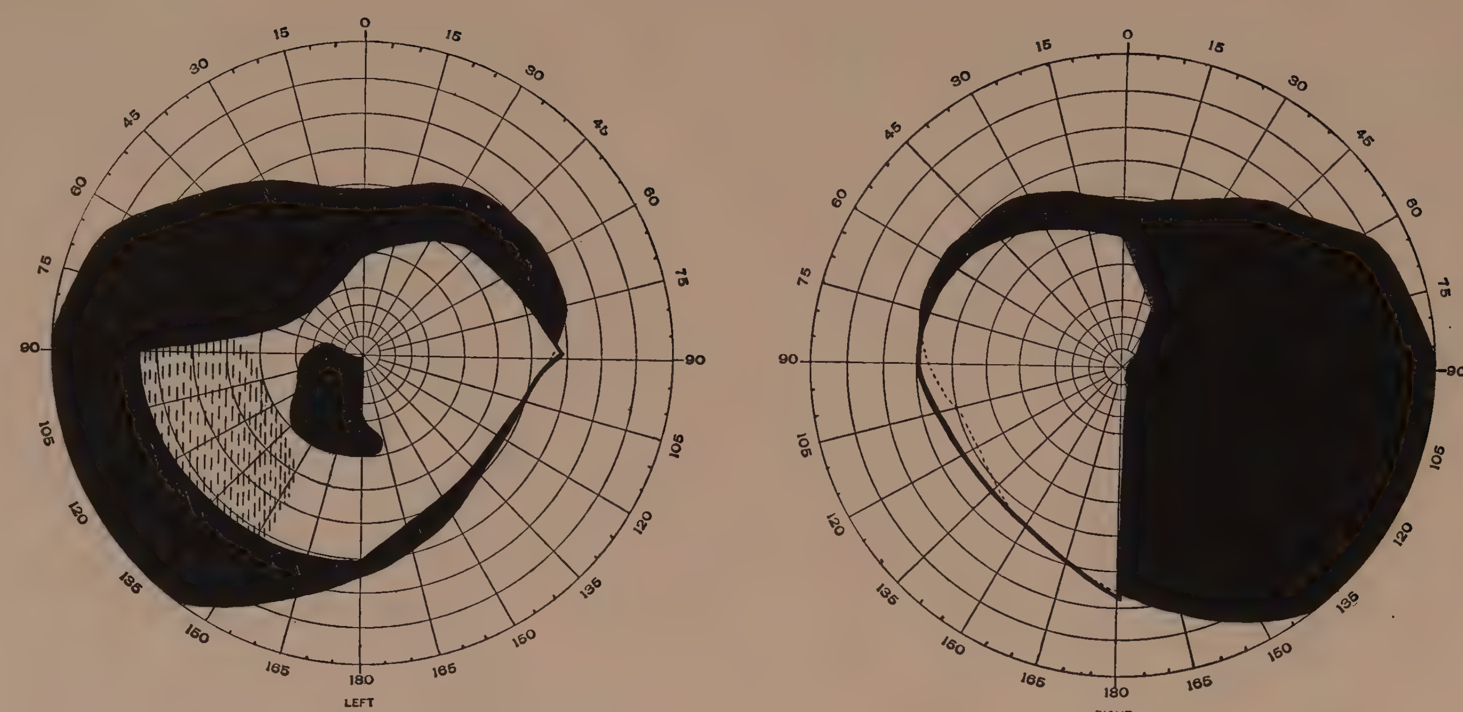


Figure 20. Fields continued as before, two months later; all color perception lost; practically complete temporal hemianopsia, right field, vertical meridian does not bisect macula; left field darkening, especially above, and paracentral scotoma shifted in position and greatly enlarged; macula not entirely covered. O.D. $V=\frac{6}{7.5}$; O.S. $V=\frac{6}{4.5}$

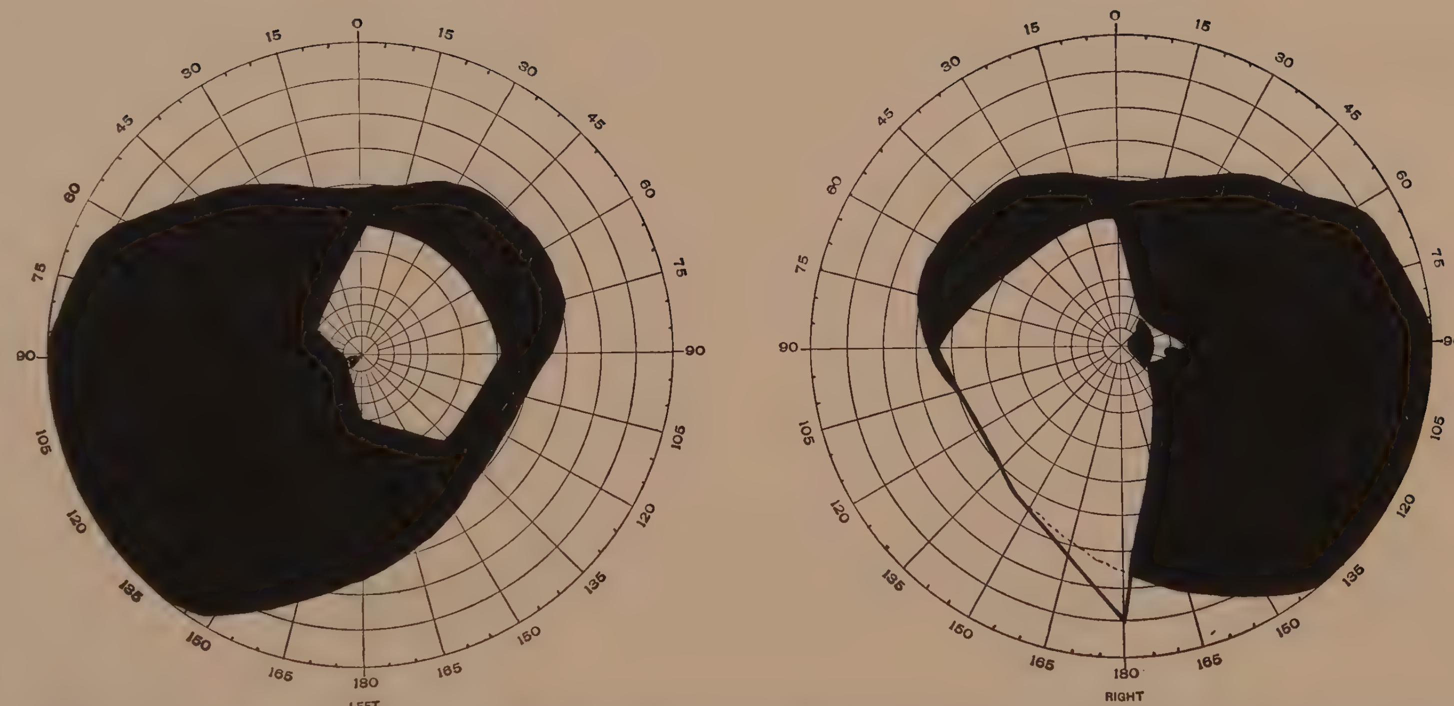


Figure 21. Fields continued as before, one month later; no color perception; right temporal hemianopsia, not quite reaching dividing line and not quite blended with scotoma; some shrinking of upper and nasal field; left temporal hemianopsia; the large scotoma and darkening outer field have blended, macula not quite covered in. O.D. $V = \frac{6}{6}$; O.S. $V = \frac{6}{45}$

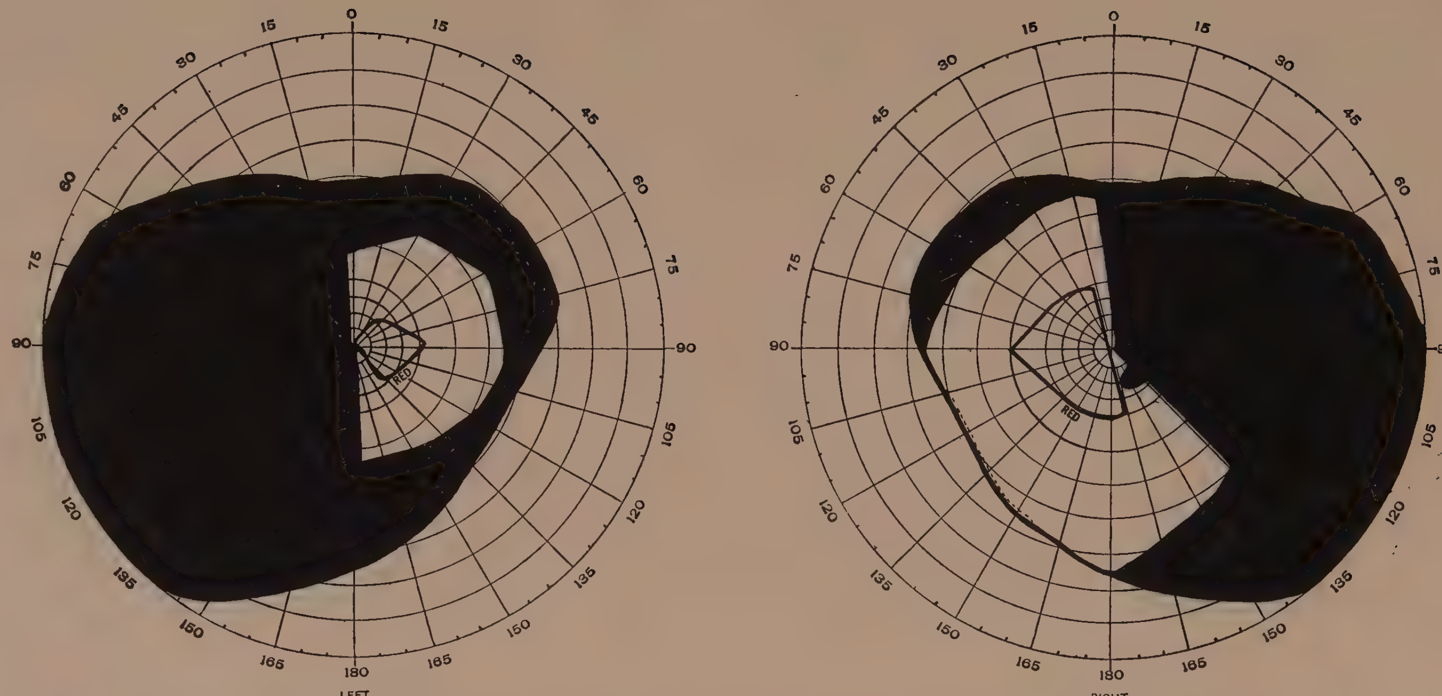


Figure 22. Fields continued as before, two months later; perception of red renewed in nasal fields; right white field recovering from below; left complete temporal hemianopsia for white, and preserved field shrunken. O.D. V$=\frac{6}{6}$; O.S. V$=\frac{6}{150}$

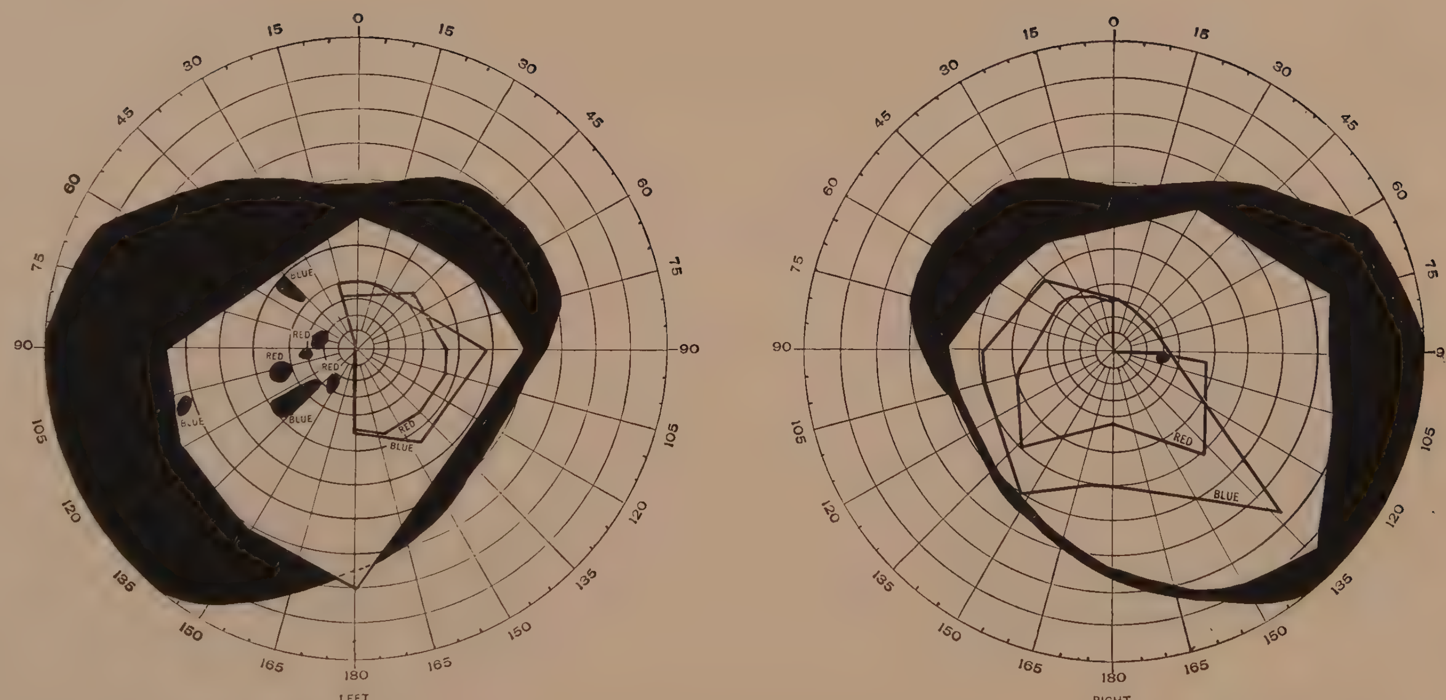


Figure 23. Fields continued as before, nine months later; right white field much restored; blue temporal slant, upper temporal quadrantic defect for red; left white field recovering, especially below; left, color (temporal) hemianopsia, but islands of color perception in temporal field. O.D. V = $\frac{6}{15}$

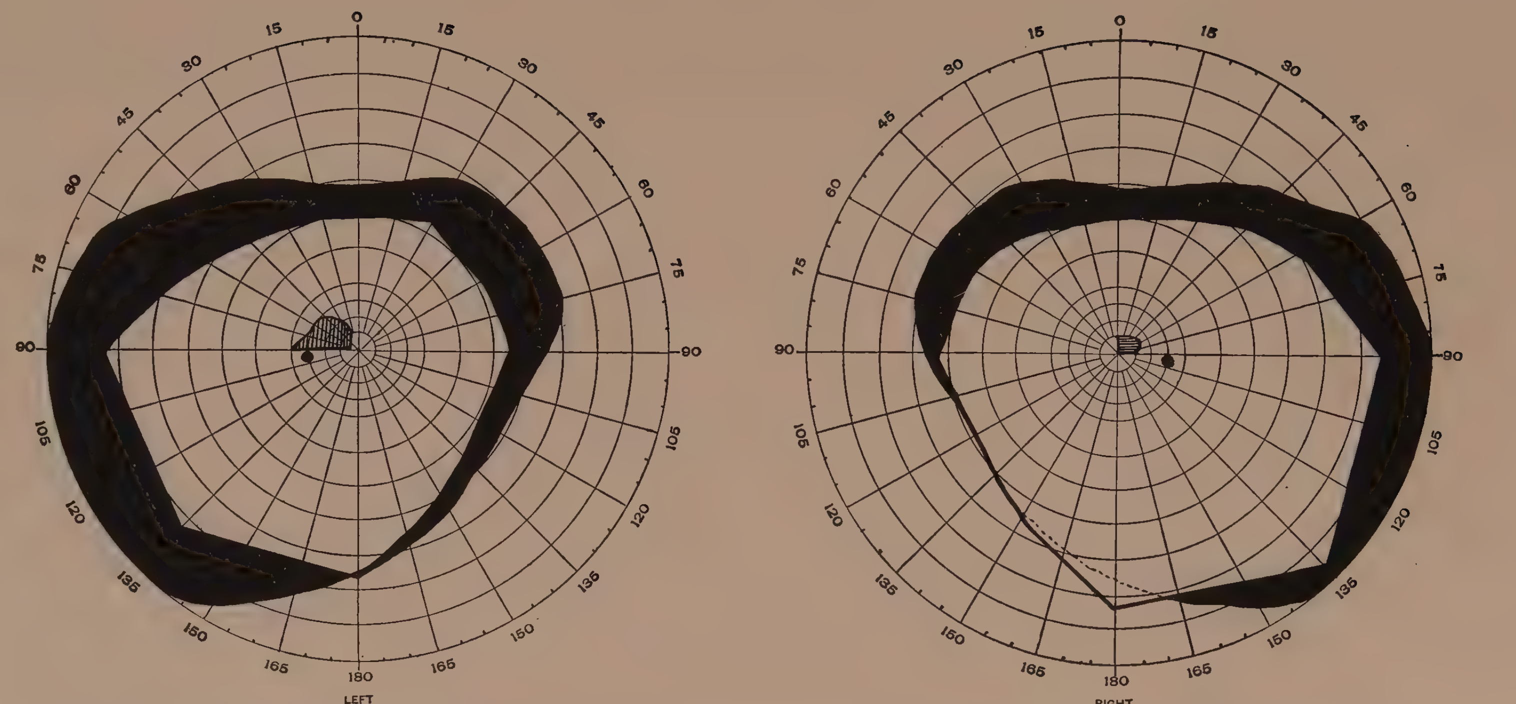


Figure 24. Fields continued as before, three months later; right white field closely approaching normal standard, faint relative scotoma up and out lingers; left white field partly restored; relative scotoma up and out (original position) lingers; colors not reproduced. O.D. $V=\frac{6}{5}$; O.S. $V=\frac{6}{12}$

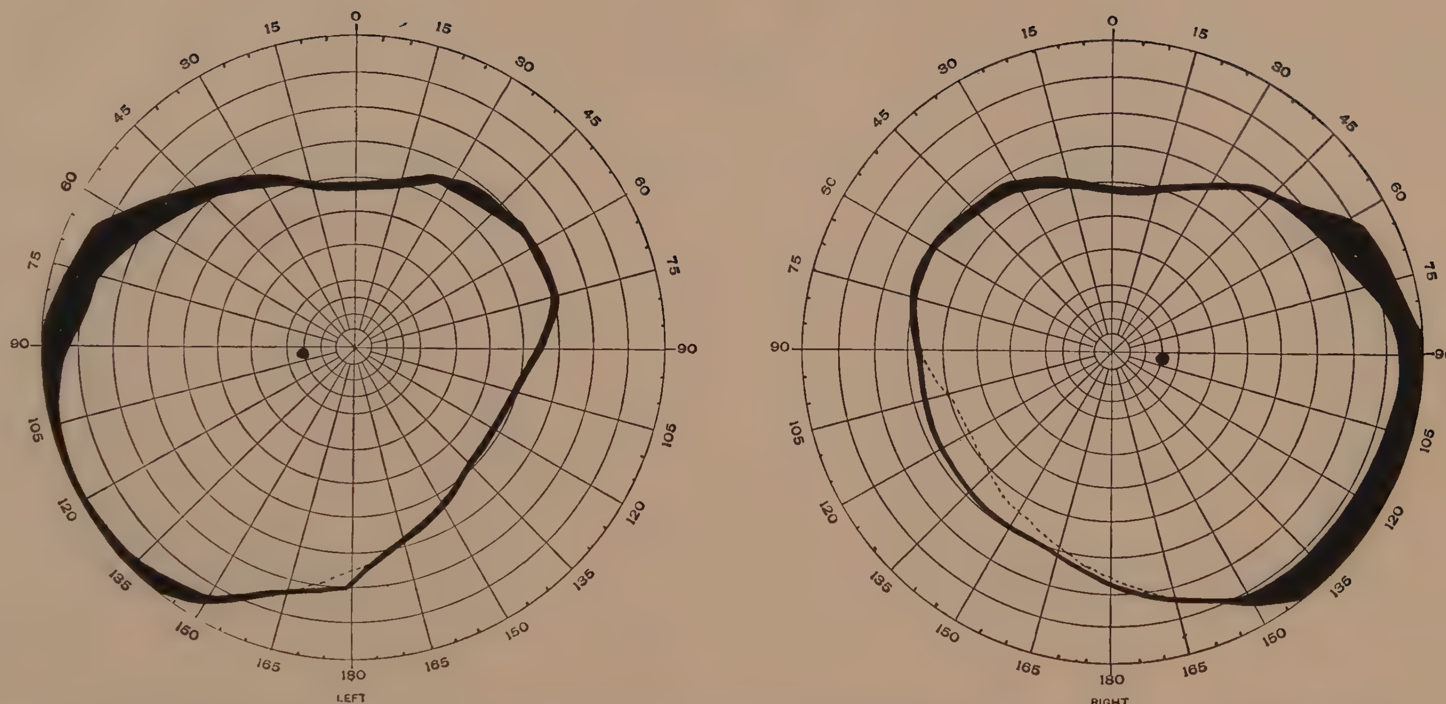


Figure 25. Fields continued as before, one year later; no scotomas, fields (white) of practically standard extent (colors not reproduced). O.D. $V=\frac{6}{5}$; O.S. $V=\frac{6}{5}$. Figures 17 to 25 represent a series in a single case

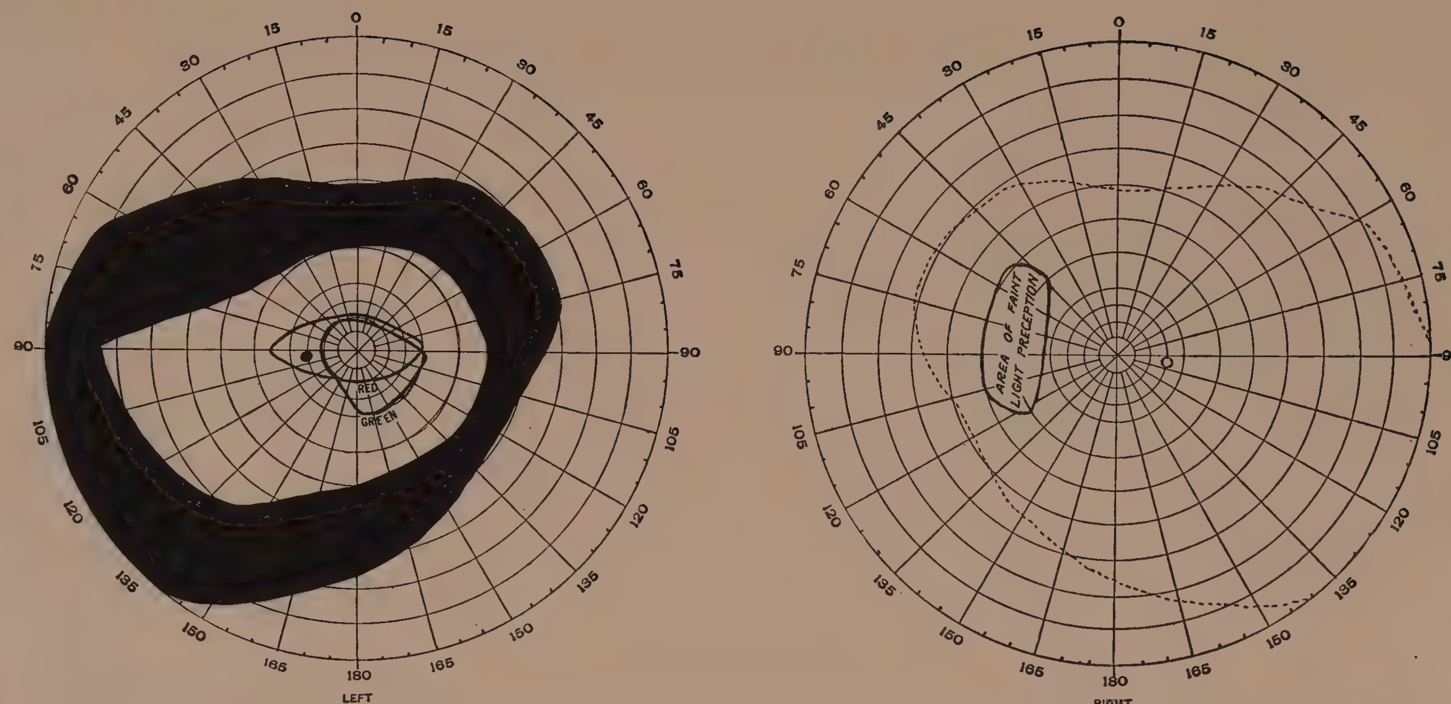


Figure 26. Pituitary body struma. Right eye blind save only an area of very faint light perception in nasal field; left field contracted and showing "temporal slant;" tendency to loss of temporal field for green

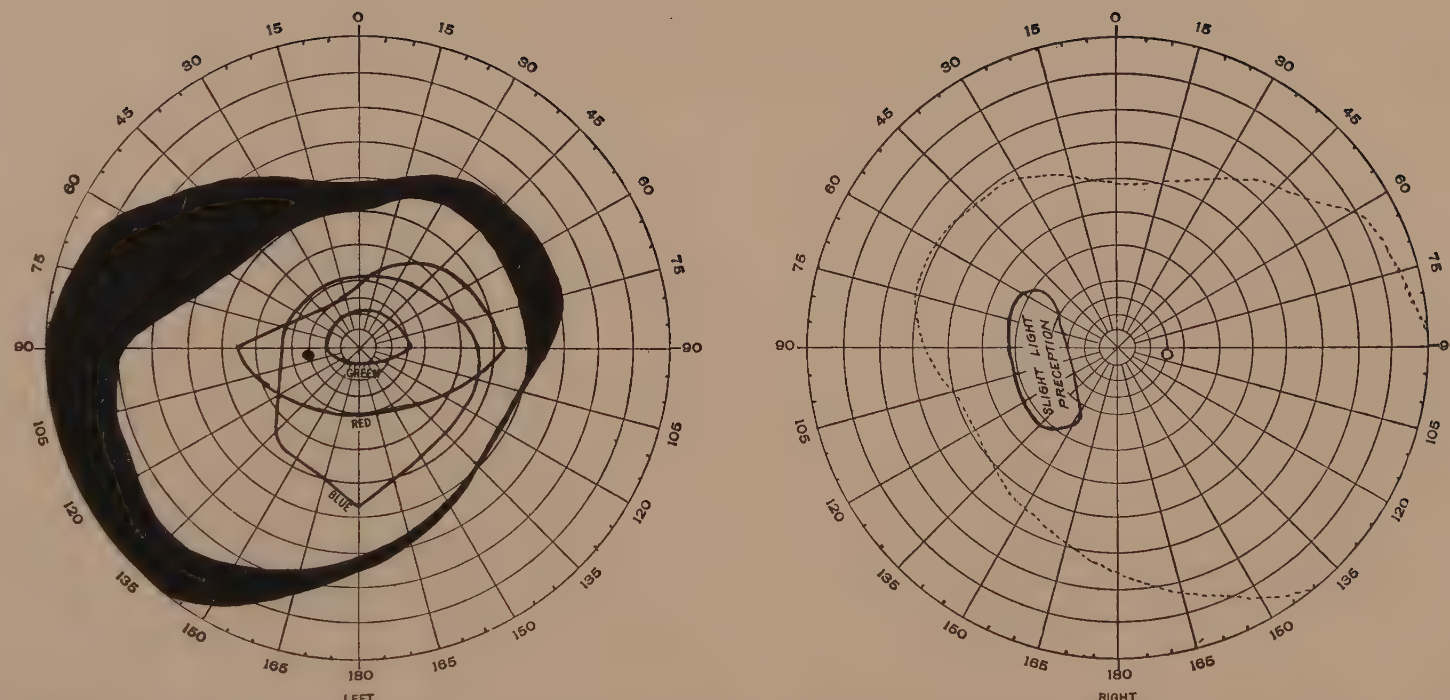


Figure 27. Visual field of same patient as depicted in Figure 26, one month after sellar decompression by Dr. Frazier; field (white) enlarged below; increase in size of color field, but slanting and slight notching of red field; no change in left field

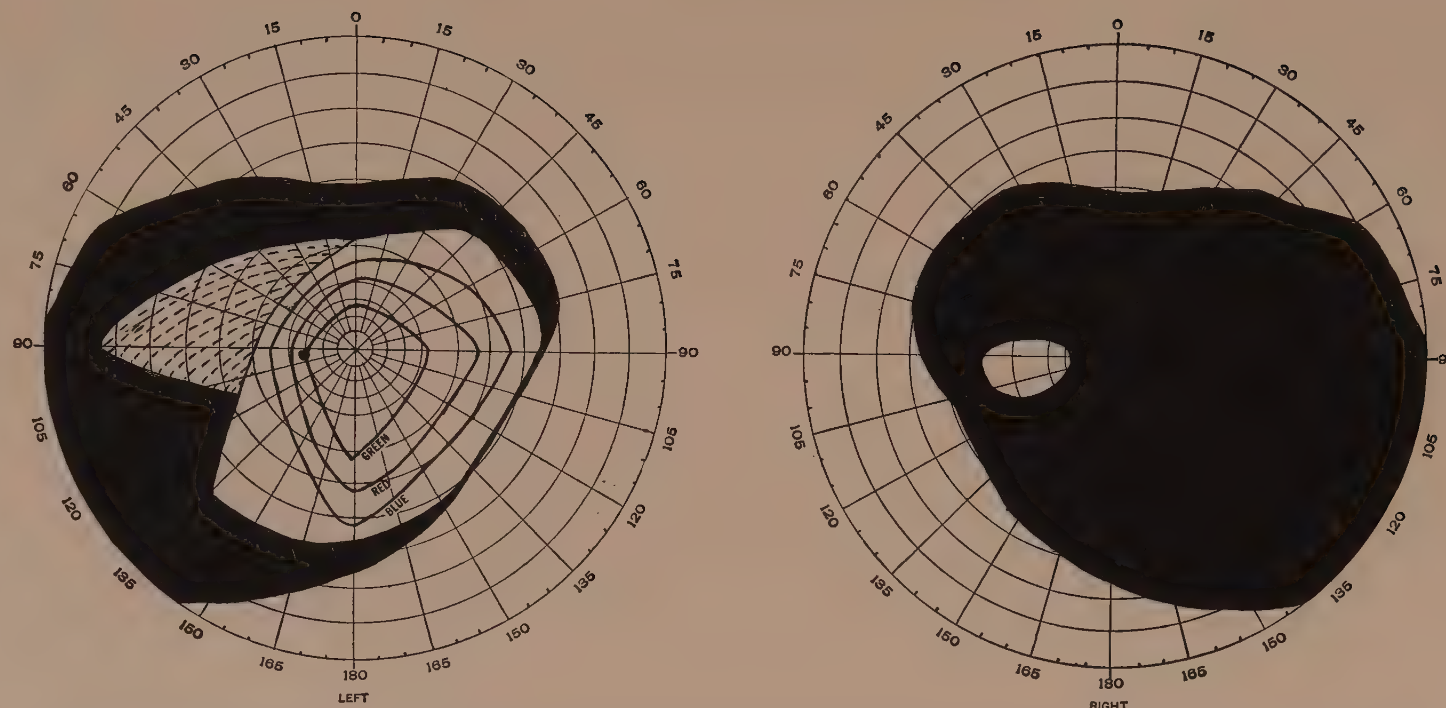


Figure 28. Pituitary body struma. Right eye blind except a small area of light perception in nasal field; left field shows marked encroachment from above producing a decided temporal slant, capped by an area of faint light perception, but no color quadrantic defect

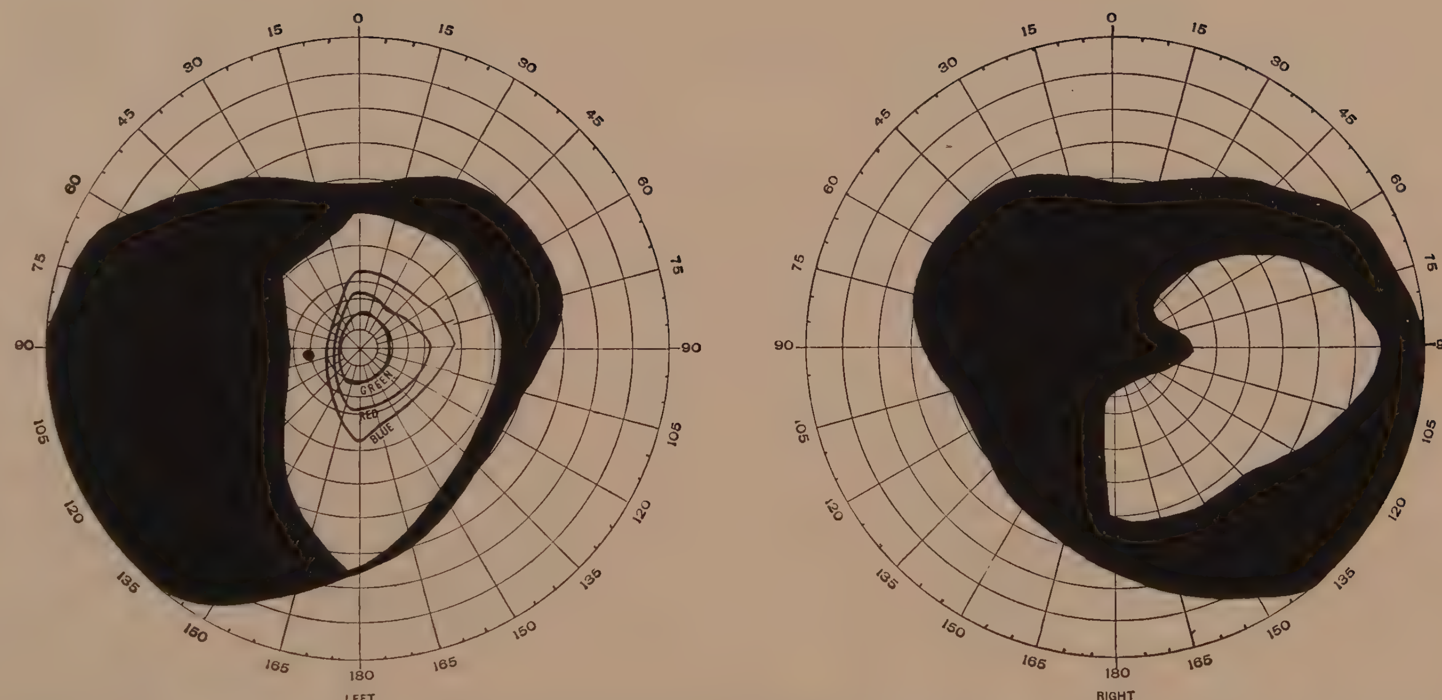


Figure 29. Pituitary body tumor. Left lateral hemianopsia, with loss of macular area in right field; left color hemianopsia; partial hemianopsia, white. Before operation

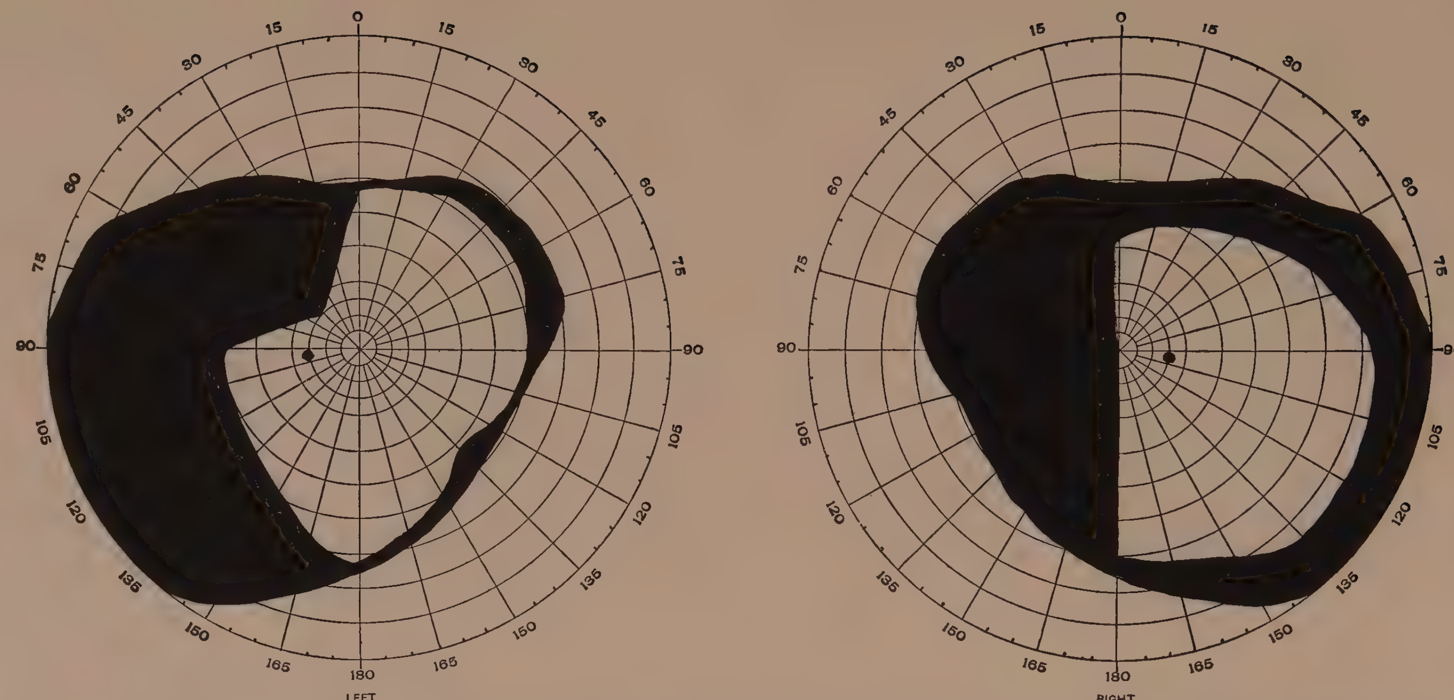


Figure 30. Fields of same patient as depicted in Figure 29 one month after sellar decompression by Dr. Frazier; field of left eye enlarging, especially from below; right field still hemianopic, but macular area restored

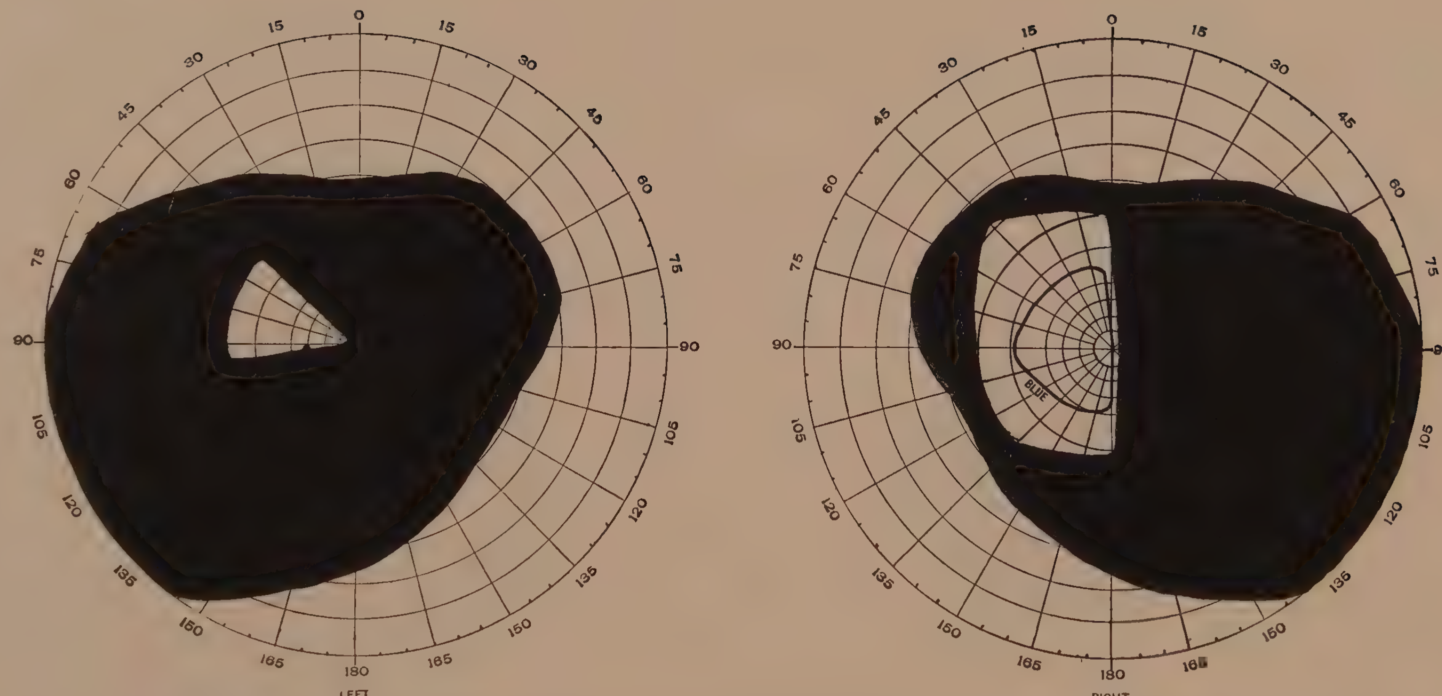


Figure 31. Tumor of hypophysis. Right temporal field loss, complete, no red or green sense, dividing line does not bisect macula; small area of light perception in left temporal field; evidently originally a right lateral hemianopsia

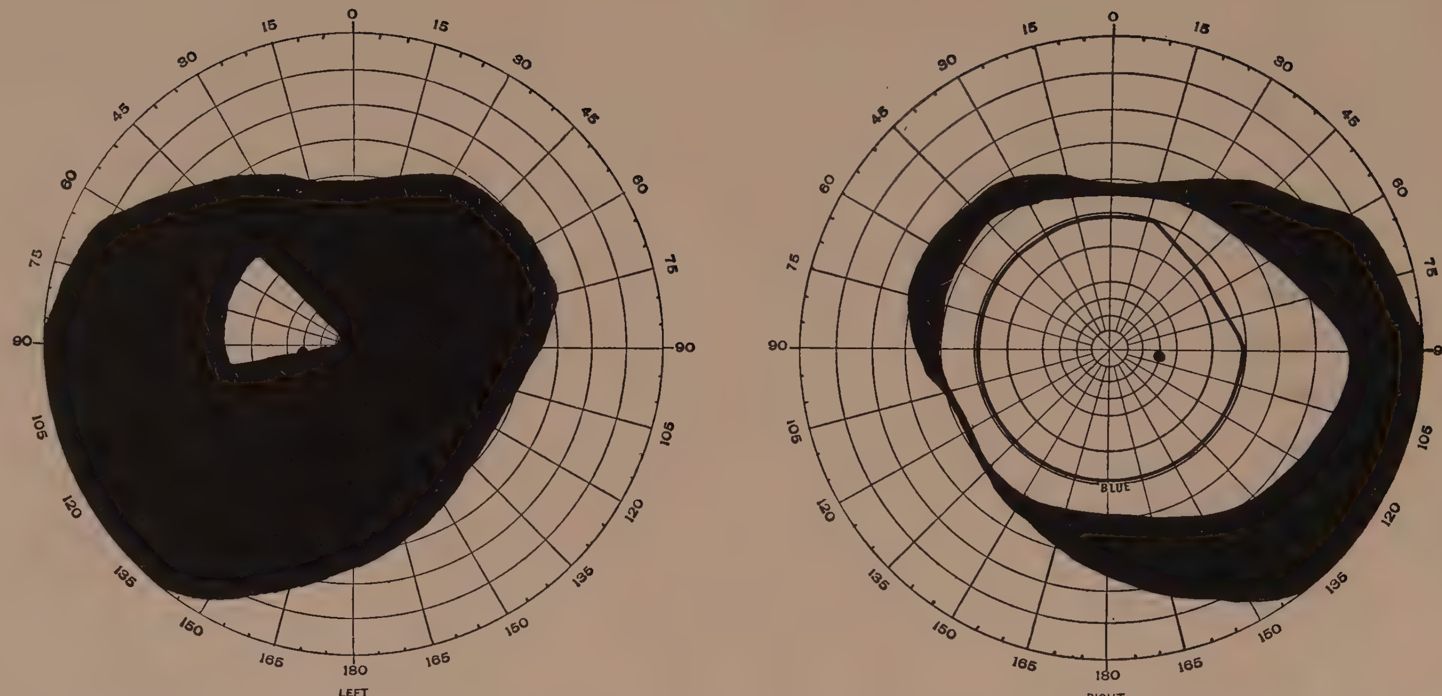


Figure 32. Fields of same patient as Figure 31, after sellar decompression by Dr. Frazier; vision in right field rose from $\frac{6}{15}$ to $\frac{\text{[illegible]}}{9}$, restored blue field, marked increase in size of white field; no change in left field

upwards. This form of restoration has been admirably studied and depicted by Cushing and Walker (8), who state: "The recession of the defects (visual field defects) takes place in a sequence the reverse of that which characterizes the stages of an advancing process."

Holloway and myself (2), in our investigation of the scotomas which so frequently are present in the visual field (especially up and out) in hypophyseal lesions, were impressed with two phenomena related to them; namely, that during the evolution of the field defects they may, as it were, shift their position, and that they often "linger" when other field delimitations have disappeared. To this fact Cushing and Walker make reference as follows (8): "In the receding process relative paracentral scotomata often persist, as the functional vulnerability of the macular and paramacular fibres appears to be greater than that of the other fasciculi."

Naturally, the earlier the relief from pressure occurs, the more perfect will be the restoration of vision and the fields of vision, but if the condition is not of too long duration, as Cushing points out, and as I have observed in Frazier's service, a typical hemianopsia may disappear; even apparent blindness, if not too long in duration, may be followed by return of sight, one case of this character being illustrated in the present series.

DIRECT VISION

According to the degree of pressure on the basal visual pathways transmitted by the hypophyseal disorder, impairment of direct vision may vary from blurred sight to complete blindness. In many cases, especially of acromegaly, abnormality in the function of vision is not in evidence.

Even though vision, as estimated with the aid of test-types, is standard, in certain cases, probably in many of them, if the records were more complete, it is blurred. To this early amblyopia exact reference has been made in the beginning of this paper.

Generally, as the visual field distortion progresses, the direct vision sinks, so that by the time the second or third stage is reached (Cushing and Walker's progressing temporal defect (8)), it has sunk to one-third or one-fourth of normal. This, however, is not always the case; even in the presence of complete hemianopsia, where

the vertical line does not bisect the macula, and where this area is not covered with a scotoma, standard, or nearly standard, vision may obtain. But usually direct vision and its degradation maintain a rather close relation to indirect vision, and its increasing distortion.

It is probable that early amblyopia is due to the vulnerability of the macular and perimacular bundle, which is easily insulted by pressure or traction, and is the last tissue of the chiasm to forget, — witness the persistence of paracentral scotomas during a "receding process."

INTRAOCULAR OPTIC NERVE ALTERATIONS

Visual disturbances and nerve-head changes are much more frequent in patients with primary hypopituitarism than in acromegaliacs, and in the majority of cases of hypophysis tumor with visual field defects (hemianopsia, etc.) the ophthalmoscopic appearances, if they are not negative, are those of so-called simple atrophy, i.e., partial or complete atrophic discoloration of the discs. Indeed, if the affection has existed for a considerable time, they are seldom absent. Choked disc is recorded by Uhthoff (13) in 9 per cent of his collected cases, and optic neuritis in about the same proportion. This percentage is decidedly higher than that developed by my own examinations. In the late stages, as Cushing points out, increase in the size of the tumor may cause increase in general cerebral pressure, with resulting hydrops of the ventricles and therefore disc edema, which may be implanted upon an atrophic nerve. This I have observed a few times. As we all know, internal hydrocephalus may give rise to symptoms closely simulating those of pituitary body disease. If the tumor mass surrounds and constricts the nerves, their sheaths cannot be distended by the cerebrospinal fluid, and edema does not take place. This point is made by Cushing, Traquair, and Uhthoff.

It is an important and an interesting fact that the so-called simple atrophy of the optic nerves, associated with tumors of the hypophysis, may present all of the ophthalmoscopic appearances of completeness, and yet marked improvement in vision may follow a successful operation or prolonged organotherapy. I have studied one patient (1), whose optic nerves were to all appearances totally atrophic, with absence of light perception lasting twelve days in the right eye and six weeks in the left, who regained normal vision in

each eye after several months of almost constant exhibition of large doses of thyroid extract. Marked visual improvement may occur within a very short time after sellar decompression. In these patients evidently the light impulses were blocked, but the nerve fibers, certainly not all of them, were not degenerated. Cushing has discussed this phase of the subject thoroughly, and in his laboratory I have studied some sections of optic nerves, stained according to the Weigert and Weigert-Pal method, and noted comparatively little degeneration, although ophthalmoscopically the nerves had been apparently atrophic and the visual field hemianopic. While prognosis must always be guarded, it would be very wrong to advise against operation merely because the nerve had the appearance of atrophy and the vision was lost or greatly degraded.

While it may not be possible, with the ophthalmoscope, to make a diagnosis of so-called *simple atrophy* of the disc of hypophyseal origin, and while this variety of nerve-head discoloration sometimes resembles that produced by various toxic substances (the toxic amblyopias) and by syphilis, the papilla not infrequently presents an appearance which is at least suggestive. Cushing and Walker (8) speak of a "glistening pallor of the nerve," and in a report from the Mayo Foundation (21), a "peculiar waxy pallor without shrinkage," is referred to as "practically a diagnostic feature."[5]

The comparatively even distribution of the pallor of the nerve-head[6] and its somewhat waxy appearance, with a suggestion of yellowish tint, are well-recognized characteristics, and even when associated with paracentral scotomas and hemianopic defects, may be the interpretation of pressure and not of true atrophy, and represent the type of the condition which recovers if the pressure is permanently released. Later, should true atrophy supervene, shrinking is evident, and sometimes the appearances are not unlike those pro-

[5] A number of symptoms pertaining to the eyes in pituitary body disorders have not been discussed; the most important of these are palsy of the exterior ocular muscles, nystagmus, exophthalmos, visual hallucinations, chromatopsia, especially cyanopsia, persistent photophobia, thickening and pigmentation of the eyelids, and hypertrophy of the palpebral glands.

[6] It is, however, true that in a number of cases the temporal side of the disc is paler than the nasal. Hirsch (9), indeed, maintains that the pallor of the papilla is regularly more pronounced on the temporal than on the nasal side.

duced by methyl alcohol. In these latter circumstances restoration of vision is not possible. It is always advisable to study the nerve-head by means of a reflecting (not electric) ophthalmoscope, and also by means of the indirect method, as was long ago insisted upon by Gowers in the investigation of color and other changes in the papilla. (Colored diagrams.)

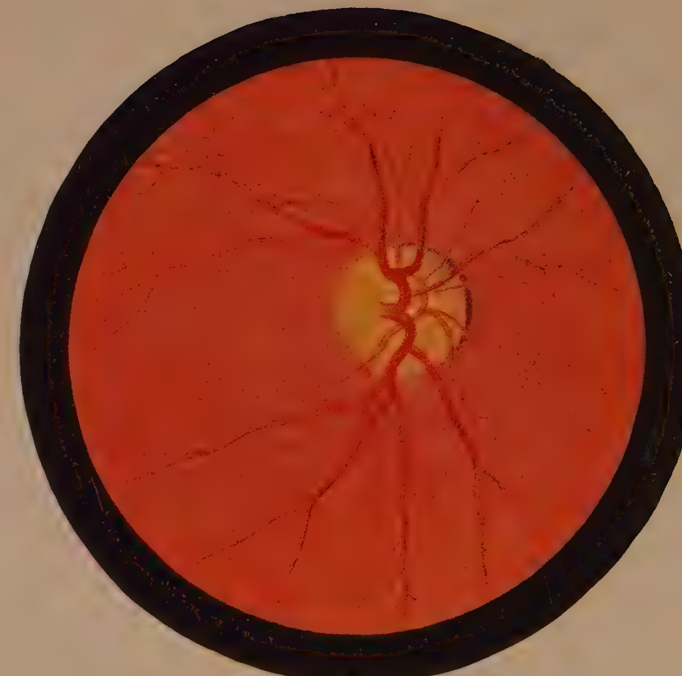
TREATMENT

To the various forms of operative procedures performed for the relief of hypophyseal lesions, with the use of X-ray and radium therapy as an adjunct to surgical interference, or without it, I shall make no further reference. The discussion of this phase of the subject is the province of the neurological surgeon. But I shall say a few words in regard to glandular therapy, often, it would seem, too optimistically recommended, and sometimes too pessimistically deprecated.

In a characteristically able paper, Cushing (22) writes: * * * * * "and should he (the physician or surgeon) venture to try glandular therapy he must be slow to draw conclusions from the apparent effect of glandular extracts given by the mouth, particularly when more than one is given at a time * * * * * The experience with pituitary extract in diabetes insipidus shows that the substance acts only when given hypodermically, and we have very little evidence that other glandular extracts have any action when given by the mouth * * * * * Most of them (glandular extracts) contain a certain amount of thyroid extract, which possibly is the only one of these substances having any definite action when given by the mouth." I have no intention to elaborate around these quotations a discussion of the value of glandular therapy either *pro* or *con*, but simply to restate my personal experiences in a few instances of dyspituitarism, elsewhere reported in detail (1).

Case A. An unmarried white woman, aged thirty-nine, with tumor of the pituitary body, demonstrated by X-ray examinations, had complete bitemporal hemianopsia, ophthalmoscopic optic nerve atrophy (very pallid discs), left complete oculo-motor palsy, absolute blindness lasting twelve days in the right eye and six weeks in the left. Under the influence of large doses of thyroid extract, asso-

LEFT EYE



RIGHT EYE

Optic nerve atrophy in pituitary body adenoma. Note waxy appearance and faint yellowish tint

ciated with inunctions of unguentum hydrargyrum, the vision of the right eye was completely restored and that of the left eye partly restored $\left(\frac{6}{9}\right)$, and the hemianopsia, ocular palsy (except that of the ciliary muscle) entirely disappeared. Constitutional syphilis was not demonstrated, either by the history or by any method of examination. During a period lasting from June 1 to October 3, the patient took 400 5-grain tablets of thyroid extract, and received 60 1-drachm inunctions of mercury; intermittently from August to October, iodide of potassium was exhibited (exact dosage not known). During three weeks prior to beginning the thyroid feeding the patient had taken iodide of potassium, protiodide of mercury, and received a few inunctions, but none of the remedies in large doses. For six months after the completion of the thyroid-mercury medication recorded above, the patient continued to take irregularly thyroid extract and to have mercury inunctions, but as she was not under my constant observation, I am unable to state accurately how much additional mercury and thyroid extract was administered. The final good result recorded was noted at the end of this period. No evidence of syphilis.

Case B. An unmarried white woman, aged fifty-one, with tumor of the pituitary body, demonstrated by X-ray examination, had complete bitemporal hemianopsia (preceded by hemianopic scotomas and color hemianopsia), reduction of visual acuteness (O.D. $\frac{6}{60}$, O.S. $\frac{40}{100}$, lowest ebb), and ophthalmoscopic optic disc atrophy; no muscle palsies. During a period lasting from June 10, 1914 to December 10, 1914, she took 400 $2\frac{1}{2}$-grain tablets of thyroid extract, and 200 $2\frac{1}{2}$-grain tablets of pituitary body extract, and received 58 1-drachm inunctions of unguentum hydrargyrum. Vision of O.D. now $\frac{6}{7.5}$, but vision of O.S. reduced from $\frac{6}{12}$ at first examination to $\frac{4}{100}$. Thyroid-pituitary body extract was continued, but no more mercury given. From July, 1914 to February, 1917, she consumed 2,100 tablets ($2\frac{1}{2}$ grains each) of thyroid extract and of pituitary body extract, because, although vision was practically restored nearly

two years before, if these medicines were discontinued, headache returned. No history of syphilis and none was demonstrated by laboratory tests.

Case C. An unmarried woman, aged eighteen, with tumor of the pituitary body, not absolutely demonstrated by X-ray examination, in that the report was "sella ill-defined and cloudy," with periods of diplopia for at least a year, moderate choking of each disc (2.5 D.). When examined complete blindness of the right eye (lasting one week), and vision of left eye reduced to counting fingers in the temporal field, the nasal field being entirely dark, but the temporal field for form intact. At the expiration of forty days of active medication, during which time she took 200 grains of thyroid extract, and received 30 1-drachm inunctions of mercury, vision was restored, $\left(\frac{6}{10}\text{ each eye, }\frac{6}{7.5}\text{ both eyes}\right)$, the choked discs had disappeared, the surfaces of the discs being pale, and the visual fields normal. History and laboratory tests negative in so far as syphilis was concerned.

A number of reports are on record of the relief of the symptoms of hypophyseal disorder as the result of glandular therapy (Elsberg, Timme, and others in America, as well as physicians abroad), or at least improvement was coincident with the administration of glandular extracts. Two of the patients whose histories are summarized were unquestionably the subjects of dyspituitarism; in one of them the interpretation of the signs is not quite clear, and the case may be omitted from further consideration. Each of the patients selected received, in addition, in the one instance to thyroid extract alone, and in the other to thyroid and pituitary body extract, large doses of mercury by inunction; neither of them, if laboratory tests and clinical history can be trusted, was a syphilitic subject. In each the cure was perfect and has remained so for a number of years. What the influence of mercury was in these cases, (assuming, as I think it is proper to assume, that the patients were not luetic), I do not know, — an increase of the so-called antiphlogistic action of mercury by virtue of the action of the gland extracts, a synergic action in that the mercury and extracts aid each other in stimulating glandular secretion, with advantage, therefore, in conditions of glandular insufficiency, have been suggested. Timme (23) believes

that thyroid administration enhances the effects of specific treatment; but there is no reason to believe that either of these patients was syphilitic.

All that I can say is, and on this I insist, that in any case of established or suspected disorder of the pituitary body the patient should be studied by the neurologist, the surgeon, the ophthalmologist, and the roentgenologist. As the result of such a conference the measures of relief must be decided. If operation is declined (as it was by both of the patients described), glandular therapy should certainly be tried, and if my limited experience, but none the less happy one in these instances, is worth anything, mercury should be added to the treatment. It is hardly necessary to say that in other cases I have tried these combinations without beneficial results.

CONCLUSIONS

The chief object of this paper, in addition to its effort to bring into review the evolution of some of the most prominent ocular symptoms of pituitary body disorders, concerns itself with an attempt to establish an early diagnosis, that is, before serious visual degradation develops.

It is surprising, to quote Charles H. Frazier (24), how late in the course of the disease the true nature is revealed. This surgeon, in looking over his records, found that when he was first consulted, 45 per cent of the patients had practically or entirely lost the sight of one eye, and that 6.5 per cent of the patients were totally, or nearly, blind in both eyes. In many of these instances had the patients come in early periods of their difficulties, there is no question that sight could have been saved.

A large number of patients with hypophyseal lesions first consult the ophthalmologist because their conspicuous symptoms are ocular, but unhappily, wait only too often until field distortions and disc-pallor or atrophy are far advanced. Fortunately, in comparatively recent times pituitary headaches are coming in for a share of attention which they richly deserve, and if the suspects are carefully examined (vision, fields, X-ray, etc.), future statistical groupings will contain the records of early cases, and the degradation of vision will be prevented.

It is probable, certain notable conditions excepted, that a definite period of time must elapse before a hypophysis lesion causes defective vision, disc-pallor and gross visual field changes, — perhaps several months. But I am well persuaded that the early amblyopia to which I have several times referred is destined to be more often recognized, and I am further persuaded that proper field examinations by modern methods are sure to detect pituitary body affections which have only too frequently escaped recognition until the grosser defects have developed.

Cushing and Walker (8), in their well-known paper, which has so frequently been quoted, say: "Detailed perimetry with small test objects of serial sizes, particular attention being paid to the shading off of the upper temporal peripheries and to the presence of relative paracentral scotomata in the same quadrant, is advocated for patients with pituitary disease in order that stages of hemianopsia antecedent to those usually recognized may be detected."

To this I would add that patients with persistent headache, unrelieved by optical therapeutics, or unexplained by definite nasal, gastric, toxic, or systemic conditions, must be subjected to "detailed perimetry with small test objects," and to X-ray examination. Many years ago, at the instance of Weir Mitchell, I investigated all of his patients coming to the Infirmary for Nervous Diseases in Philadelphia with what it was the custom to call "chronic headache," with the aid of a perimeter, and found visual field changes. But the findings were not correctly interpreted, and the methods were comparatively crude. Doubtless in a number of these cases pituitary involvement was overlooked, as well as other conditions creating increased intracranial pressure. Now our methods of examination are greatly improved and our technique largely refined. What is necessary is to insist upon a more general use of these methods and the employment of this technique.

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PLAGUE IN THE ORIENT WITH SPECIAL REFERENCE TO THE MANCHURIAN OUTBREAKS

By

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INTRODUCTION

Plague is essentially an Oriental disease, and whether Dr. W. J. Simpson is right or wrong in naming China's southwestern province of Yunnan as its primary focus of infection, there is no doubt that since the great pandemic of 1894 the endemic areas have increased both in number and extent. The vast Empire of India with its 320,-000,000 people may be considered permanently infected, although certain administrative areas like the Punjab, the Presidency of Bombay, and the United Provinces of Agra and Oudh suffer to a greater extent than the hilly province of Assam, where during the last six years only one case has been recorded. During the last eighteen years, over ten million persons have died of plague in India alone. In other parts of Asia frequent outbreaks of plague have occurred during recent years, e.g., Ceylon, Straits Settlements, Dutch East Indies, Siam, Indo-China, Japan, Hongkong, the provinces of Kwangtung and Fukien (particularly at the ports of Canton, Swatow, Amoy, Foochow), Manchuria, and Siberia. The coal mining center of Tongshan three hours by rail from Tientsin was infected by some bubonic cases from Hongkong in 1898 and lost a thousand lives in four months. The port of Newchwang (Yinkow) in South Manchuria was invaded in 1899 (probably through vessels from the south) and lost in five months 2,000 people. From 1901 to 1903 isolated cases were detected, but they never resulted in an epidemic. It is strange that the great pulmonary epidemics of 1911 and 1921 did not touch either Tongshan or Yinkow, although both lie on the main highway of railway traffic.

Although favorable results have been obtained by the application of modern preventive methods in such places as the Philippines and Japan, the total suppression of bubonic plague appears to be an ideal still to be achieved by interested governments. The following

mortality figures show how widespread the disease is in different parts of the Orient (Table 1).

Passing on to China, we find that statistics are difficult to obtain from any part except Shanghai and Manchuria, the former controlled by an efficient Health Department of the International Municipal Council, the other by the Manchurian Plague Prevention Service. Shanghai with a population of close to a million reported

TABLE I

Plague Invaded Areas in the Orient

Location	Years	Year of Severest Infection	Total Plague Deaths	Aggregate Population
India	1896–1917	1907	9,841,396	320,000,000
Ceylon	1914–1917	1914	978	800,000
Straits Settlements	1910–1917	1917	280	1,000,000
Dutch East Indies	1911–1917	1917	34,732	40,000,000
Siam	1911–1917	1916	1,063	9,000,000
Indo-China (French)	1911–1917	1913	14,911	18,000,000
Hongkong	1895–1917	1914	15,731	520,000
Japan	1907–1916	1907	1,380	50,000,000
Formosa (Japan)	1896–1917	1901	24,108	3,400,000

only sixty-one human cases and 1,108 infected rats in the years 1910–19. The years 1916–19 were entirely clear.

In the two southern provinces of Kwangtung and Fukien, epidemics of greater or less severity occur almost yearly, but up to the present no reliable records have been published. It is hoped that with the recent establishment of a Ministry of Health attached to the Southern Government, headed by a responsible medical man, we may look forward to more accurate information during the coming years.

The incidence of plague in a country or community seems to depend as much upon its location, climate, humidity, and the character of its inhabitants, as upon the preventive measures employed. For instance, as far as India is concerned, the mortality curve reaches its highest point in March and its lowest in July. This periodicity

has been demonstrated to be due to the humidity of the earlier months of the year, since humidity is favorable to the life of the flea. In spite of the efforts of the government to deal with native prejudice, and the well-directed measures to control the malady, it has continued to rage from year to year with almost unabated severity up to the present time. On the other hand, we see steamer traffic taking place regularly between the endemic southern ports of Canton, Hongkong, etc., and northern ports like Shanghai, Dairen, Chefoo, Tientsin, Newchwang. Yet plague seldom visits these places, although there must be large numbers of infected rats in the holds of the steamers, and ordinary anti-rat precautions such as disc guards and tarred ropes are not rigidly enforced when these ships are moored beside the wharves.

With the exception of some accidental cases, the epidemics referred to above have been of a bubonic nature, propagated by means of and through the agency of the rat flea. As found in India, whenever the seasons are most humid, fleas abound and the incidence of bubonic plague becomes greater. The prevention of plague in these regions therefore lies principally in the destruction of rats, the rat-proofing of houses, and the proper supervision of possible rat-infested merchandise, especially grain, which certain authorities regard as more dangerous vehicles of infection than human beings.

THE MANCHURIAN OUTBREAKS

When we turn to the series of epidemics known as the Manchurian outbreaks, we deal clinically and epidemiologically (except that the causative organism is the same) with a totally different disease. In this type of plague the rôle played by the rat and its appendage the flea is negligible, beyond the fact that the early cases are probably secondary manifestations of the bubonic infection in the lungs, which in a favorable environment, such as is met with in the crowded semi-underground inns of North Manchuria, readily follows a purely pulmonary course. It is quite possible that the tarabagan or Mongolian marmot (*Arctomys bobac*), found in large numbers on the Siberian and Mongolian plains, may, like the domestic rat, harbor the plague organism and that it is the real precursor of epidemics of plague pneumonia. Our latest experiments on these animals, which

will be mentioned later, seem to support this view. So able an observer as G. W. McCoy (1) has stated, "Pneumonic plague in man rarely occurs from rat infections, and it is an interesting and possibly significant fact that in plague squirrels there is a very definite tendency to pulmonary localization, a condition which never occurs in plague in rats."[1]

Russian observers have steadily clung to the idea that plague arises from the skinning and eating of tarabagan flesh, so that whenever a case is reported in Siberia, the comment, "after having partaken of the flesh of tarabagan," inevitably follows. At the time of writing (August 20, 1921), some new cases of bubonic plague have just been reported from Dauria in the Transbaikal regions, the first two being a Russian station master and a signal man, who respectively developed a cervical and an axillary bubo after having skinned and eaten tarabagan flesh. Careful inquiries made by our medical officer on the spot have elicited the information that these two men skinned as well as ate the flesh while four others who only ate the flesh did not fall ill. Three more cases have been reported in that region, including a doctor who operated on the bubo of the station master and developed plague septicemia. It will be interesting to see whether any pulmonary cases will result from this local outbreak, as we may then have some ground for connecting the tarabagan with pneumonic plague in man. My own researches in Mongolia in 1912 failed to record a single authentic case of direct tarabagan infection in man, and until further evidence is produced one is obliged to come to the conclusion that the Manchurian epidemics have arisen as a result of primary bubonic infection invading the lungs in addition to other organs. Whether the wild tarabagan or the domestic rat plays the more important rôle in disseminating the disease in this endemic region must still be worked out, and it must be confessed that our attempts at finding infected rats in Manchouli, Hailar, Harbin, and Mukden (all situated in Manchuria) have been as devoid

[1] This statement will require modification in view of some interesting localized pneumonic-plague epidemics recorded: e. g., British freight steamer, *Friary*, which had eight deaths out of a crew of twenty-one in 1901; British mail steamer, *Nagoya*, which had eight deaths out of a crew of 195 in 1919; two epidemics on the Gold Coast in 1908 and 1917, and others (2 and 3).

of positive results as our attempts to find plague infected marmots in their underground quarries in Mongolia.

That the Transbaikal region is endemic for plague may be judged from Table 2. Several years ago (4) I made a summary covering the period 1898–1910, showing that plague occurred every year in the Kirghiz Steppes, a vast stretch of territory extending from Astrakhan in Europe to Uralsk and Semiretchinsk in Asia.

It will be seen from Table 2 that the three great epidemics oc-

TABLE 2

Plague Years in Siberia and Manchuria

Year	Season	Locality Where Plague Was Present	Type	Mortality
1910	Sept.	Dauria (Siberia)	Bubonic and pneumonic	40
1911	Oct.–Apr.	Manchuria and N. China	Pneumonic	60,000
1912	......	No record	......	......
1913	Aug.	Kirghiz Steppes	Bubonic	Not ascertainable
1914	Oct.	Transbaikalia	Bubonic	13 (out of 16)
1915	......	No report	......	......
1916	Sept.–Oct.	T'aochow in Kansu	Pneumonic	About 60
1917	Sept.–Dec.	South Mongolia	Bubonic and pneumonic	Not ascertainable
1918	Jan.–Apr.	8 provinces: S. Mongolia, Suiyuan, Chahar, Shansi, Chihli, Shantung, Anhwei, Kiangsu (offshoot of 1917)	Pneumonic	16,000
1919	Sept.	Ikievkaya (Transbaikalia)	Bubonic	2
1920	Sept.	Abagatui (Transbaikalia)	Bubonic	5 (out of 6 cases)
1921	Jan.–May	N. Manchuria, Chihli, and Shantung (offshoot of above)	Pneumonic chiefly, only 12 bubonic cases observed	9,000
1921	Aug.	Dauria, 40 miles west of Manchouli	Bubonic	5 (so far)

curred in 1910–11, 1917–18, and 1920–21, when 60,000, 16,000, and 9,000 persons, respectively, died. As I was directly responsible for the antiplague work in the first and third epidemics, I will deal with them fully here. The first epidemic found China absolutely unprepared, for until our staff arrived there were no hospitals and no proper sanitary staff to cope with the emergency. The Central Government had, however, considerable power over the provinces, and when I applied for the necessary funds, medical assistance, and permission to perform postmortems, and to cremate the dead, all my requests were rapidly granted, and by April, 1911, the whole epidemic from Harbin southwards as far as Shantung had been stamped out. When the 1920–21 outbreak came we were much better prepared. The Manchurian Plague Prevention Service had been established for nine years, and the officials and natives more or less understood the nature of our mission, so that, although some trouble was caused by unruly soldiers and the ignorant masses led by a few professional agitators, our antiplague measures met with general approval. Only four cities reported a high mortality (Manchouli, Dalainor, Tsitsikar, and Harbin), claiming 7,000 out of the total 8,500 deaths in Manchuria. The epidemic was confined to North Manchuria, practically all places south of Changchun escaped, and only 300 cases occurred in the two provinces of Chihli and Shantung.

Table 3 gives a comparison of the two epidemics showing the date of the first case reported and total mortality in each district.

As illustrating how the migration of the population affects the spread of the disease, two points may be stated. (1) In the 1910–11 epidemic there was no definite antiplague authority and no co-operation between the various railway lines operating in these areas. Sick patients and persons incubating the disease spread the infection broadcast, and thousands of victims were reported in all of the large cities between Harbin and Tsinan (Shantung). It was quite common to find a dozen cases in the trains on the South Manchurian and Peking-Mukden lines. One notorious train conveying thirty-nine sick to Tientsin and Peking was sent back to Mukden, and it was the sorting out of these cases that probably caused the death of the young Englishman, Dr. Jackson. In 1921 we made timely arrangements with the railway authorities regarding the restriction

TABLE 3

Two Epidemics Compared

City	1910–11		1920–21	
	First Case Reported	Total Mortality	First Case Reported	Total Mortality
Dauria (Siberia)	Sept.	40	......	......
Abagatui (Siberia)	......	......	Sept.	5
Manchouli	Sept.	400	Jan. 21	1,141
Dalainor	Oct. 19	120	Jan. 13	1,047
Hailar	Oct. 27	3	Oct. 22	98
Tsitsikar	Dec. 4	600	Jan. 18	1,734
Harbin	Oct. 27	9,000	Jan. 22	3,125
Hulan	Dec. 13	4,000	Feb. 7	322
Shwangchengpu	Jan. 5	1,500	Mar. 14	134
Changchun	Dec. 31	5,000	Jan. 31	77
Kungchuling	Jan. 15	35	Jan. 31	5
Mukden	Jan. 4	4,500	Mar. 29	4
Dairen	Jan. 4	66	......	0
Chefoo	Jan. 21	400	May 3	24
Tsinan	Feb. 1–7	450	......	0
Vladivostok	......	0	Apr. 9	520

and control of the passenger traffic and so saved thousands of lives. (2) In 1911 very few coolies traveled eastward from Harbin to Suifenho and Vladivostok, and hence no cases were reported at either place. In 1921, however, owing to the opium boom, 800 to 1,000 third and fourth class passengers were traveling in that direction daily to cultivate the fertile regions. Although the inspection of passengers was enforced at Harbin station, several persons incubating the disease escaped detection and developed symptoms on arrival at different towns. Fortunately, these were isolated instances, and only Vladivostok suffered to any great extent, claiming 520 deaths up to July, among them two bubonic cases. Some infections among rats were also found.

SEASONAL PREVALENCE

When we study the seasonal prevalence of the epidemic, we find that on both occasions it originated in September (the one at Dauria

and the other at Abagatui, two Siberian villages). The first outbreak continued without any interruption at Manchouli and passed on to the other cities until its suppression in the following April. The second outbreak did not show its full virulence until November, at Hailar, where I personally examined the early bubonic cases and saw the gradual evolution through the septicemic into the pulmonary form. It was the liberation of nine contacts by the local soldiers after their attack upon the Chief of Police and the escape of some to Dalainor that led eventually to the general epidemic; for in the windowless, insanitary, underground dwellings of the miners, forty to sixty of whom were herded together in double tiers within an area of 40 by 20 feet, the *Bacillus pestis* found indeed a fruitful soil. From Dalainor cases traveled to Manchouli, Tsitsikar, and Harbin, where strong measures had been taken to protect both the local people and places further south by means of the inspection of trains as well as by quarantine of the restricted number of third class passengers for five days at Changchun. The poorer members of the community, however, did not understand the value of preventive measures and refused to report cases. When anyone fell ill he was hidden until dead and then thrown out into the street at night, or else he was driven out in the last stages of the disease, with the injunction not to report his address, for fear the contacts would be sent to the observation wagons. This unnecessary fear of the anti-plague officers extended even to the educated classes, for one of the corpses picked up in the streets was identified as that of the Vice Chairman of the native medical society whose wife preferred this treatment of her dead spouse to being isolated.

SOME PROMINENT SYMPTOMS. DANGER TO CONTACTS

It is not my purpose in this address to travel over old ground but to allude to the more interesting and rarer features of the disease. Like other insufficiently studied affections, pneumonic plague grips the interest of the research worker, not only because of its extraordinary virulence, its simple direct means of infection, and its equally simple method of control (if only the human machine were not such a complex psychological and obstinate factor), but also because of the possibilities of immunization.

After an incubation period of two to six, usually three days, the patient feels drowsy and dizzy, with headache and lack of appetite. He complains of a chilly feeling and develops a moderate temperature of 102° to 103° F., and fast, soft pulse. This condition usually lasts for twenty-four hours before a cough sets in, at first dry but quickly accompanied by liquid, frothy sputum tinged with bright red blood. In a fair percentage of cases the hemorrhage is considerable, the floor and bedding being profusely covered with blood; while occasionally the patients die without experiencing any cough or hemoptysis. The period intervening between the appearance of the fever and the first sign of cough is most important for those in charge of contacts, because this is the non-infective interval when the sick may be removed without endangering the others. As soon as cough appears the danger of infection becomes greater. This is well illustrated in the case of our late Dr. Yuan Teh-mao, who was infected while serving as chief of the house-to-house inspection squads. On the fifth day after exposure, though feeling ill and probably feverish, he still attended a crowded sanitary conference of twenty-six people and moved among our medical staff the whole day. That night he was sent to bed with a temperature of 102° F., and the next morning *Bacillus pestis* was found in the scanty sputum coughed up. Not one of the sixty persons with whom he had mingled became ill. Table 4, illustrating the percentage of plague cases among contacts confined in our isolation cars at Harbin, shows how small a percentage develop the disease if properly cared for. Inci-

TABLE 4

Mortality among Contacts in Isolation Wagons

Month	No. Admitted	Sent to Hospital	Plague	Non-Plague	Per Cent Plague
Feb.	547	47	34	13	6.2
Mar.	911	118	92	26	10.1
Apr.	485	57	47	10	9.7
May	78	5	5	0	6.4
Total in 4 months.	2,021	327	178	49	8.1 (Average)

dentally, it points out that during the height of the epidemic (March and April), when the assistants were dealing with an unusual number of contacts, the percentage of infection was higher.

These figures compare very favorably with those of Dalainor, where, owing to incomplete organization and the obstinacy and disobedience of the mining coolies, 144 out of 655 contacts registered in February and March, i.e., 21.8 per cent, died of plague.

PLAGUE CARRIERS

In discussing such a deadly infection as pneumonic plague the question of carriers naturally invited our attention. The discovery of the first authentic case was accidentally made when dealing with the first group of contacts.

Chang I, aged twenty-seven, motor car driver, was admitted to Harbin Isolation Ward on February 1, with nineteen other persons from an inn where one man had died of plague. On February 2, he complained of headache and slight fever. Sputum, apparently normal, showed suspicious bacilli the same day. Cultures examined the next day were positive and the majority of the bacteria resembled *Bacillus pestis*. On February 7, this positive culture (whole agar slope) was inoculated intraperitoneally into a guinea pig. Eighteen hours afterwards the guinea pig died, and smears from heart, spleen, and peritoneum showed *Bacillus pestis*. Cultures from same organs all showed pure *Bacillus pestis*. On February 6, after the patient had been apparently well for four days, swabs were taken from his sputum and tonsils. Culture from sputum was inoculated into a guinea pig, which died twenty-four hours afterwards. Smears and cultures from spleen, heart, and peritoneum gave positive results.

One of the eighteen contacts, Wang, died unexpectedly on the evening of February 6, i.e., six days after his last contact with the first sick man. As the incubation period of pneumonic plague is seldom over five days, it is possible that Wang might have been infected by the carrier Chang who harbored the bacilli for at least a week.

After this event, twenty-four other examinations were made for possible carriers between March 1 and 30, but in only one instance did we obtain positive results.

Chang II, aged thirty, coolie, was one of four contacts examined

on March 4. Sputum appeared normal and cultures were made. Growth forty-eight hours after showed suspicious bacilli. On March 6 this was inoculated subcutaneously into a guinea pig, which died twenty-four hours afterwards. Smears from heart, spleen, and lungs were all negative, but cultures from the heart showed several colonies, and those from the spleen, one colony. Another guinea pig inoculated intraperitoneally with this heart culture died in twenty-four hours with positive findings in heart, spleen, and peritoneum.

One girl examined on March 26 also showed *Bacillus pestis*, but she developed the disease before the end of the incubation period and her case was therefore disregarded.

It is premature to say how far the question of carriers influences the course of a pneumonic plague epidemic but this is the first occasion on which the matter had been scientifically worked out and confirmed.

INFECTIVITY OF SICK ROOMS

The illness of Dr. Yuan from February 17 to 20 in our new hospital block (steam heated, with temperature maintained at 17° C.) enabled us to make the first investigation regarding the infectivity of the sick room *per se* immediately after the death of the patient. For this purpose the following experiments were made:

Twelve guinea pigs, two each in tin buckets, were placed on the wooden floor of the room (12 by 12 by 10 feet, with one large closed window) for periods ranging from one-half to four hours. Nothing was previously disturbed and the door was not opened except when the animals were removed at certain times. Only two guinea pigs died; the first had been exposed for one hour, dying on the fourth day, and the second had stayed in the room half an hour, dying on the seventh day. The other ten remained healthy. Postmortems confirmed septicemic plague with congestion of lungs in both animals.

Eight guinea pigs in lots of two were exposed on March 2 to air of sick room, one-half hour before, one-half hour after, one hour, and two hours after death of patient. One animal died on March 17 (i.e., fifteen days after exposure), showing no bacilli on smears of organs, though pure cultures from the blood were obtained.

Four guinea pigs were allowed to stay in the plague room from April 5 to 9, where six patients had successively come in and died.

One animal became sick, and on being killed showed lesions in the respiratory organs. No tonsillar or glandular infection was noticed. This experiment was performed on behalf of a Russian bacteriologist who at first believed the primary seat of infection was situated in the tonsils.

Seven other experiments were performed with ten rabbits and twenty-eight guinea pigs by placing them in sick rooms both before and after the patients had died, and also in coffins containing clothes freshly removed from the dead, but in no case did the animal die. One rabbit showed pneumococcal infection. Similar experiments were also conducted at my request in March at Dalainor by Dr. E. T. Hsieh, who exposed ten young rabbits at heights varying from 1 to 8 feet to the air of a room (10 by 12 feet) recently vacated by four dead. The animals were all living on the seventh day and afterwards.

These discoveries seem to indicate that the sick room by itself or even when occupied by plague patients is not particularly dangerous except when one is standing in the direct line of the sputum or droplet. They also raise the question as to the need of spending so much energy and money on the disinfection of houses, as well as the wisdom of burning infected quarters, which was done so extensively in the 1910–11 epidemic.

INFECTIVITY OF RAILWAY CARS

We have on record four occasions on which a plague patient suffering from fever and cough was found in a crowded railway car running between Harbin and Changchun. The first was on February 2, when a dying man with hemoptysis was discovered at Yaomen in the train leaving Changchun for Harbin. The other forty-seven passengers were forthwith conveyed to Harbin for observation but all remained healthy and after six days were liberated. The next two happened on February 16 and 20, when thirty-seven and forty-seven persons were similarly observed without subsequent illness. The fourth case occurred in the middle of March, and here also none of the thirty contacts developed the disease though all had been in the car with the sick man for over nine hours. The distance between the two cities is 150 miles.

EFFICACY OF GAUZE AND COTTON MASKS

It has been pointed out by Barber and Teague (5) that the simple gauze and cotton mask introduced by me and recommended by the International Medical Conference of Mukden in 1911 for pneumonic plague work is pervious to a spray of *Bacillus prodigiosus*. Dr. J. W. H. Chun working with *Bacillus lactis* obtained similar results. It must, however, be remembered that in the plague wards one does not stand within a distance of three feet in the direct line of the breath of the patient, and that quiet breathing or an occasional cough is unlike the continuous spray used in the experiments.

To satisfy ourselves further, we made a series of cultures from masks which had been used in the wards by the doctors and assistants for various periods ranging from one-half to four hours. The outer gauze layer, the inner gauze layer, and the intervening cotton wool were all tried. In only one sample out of fifteen investigated was a positive culture obtained, namely from the outer layer of the gauze which had been worn continuously for three hours. Nevertheless, in view of Dr. Yuan's accident, we considered it best to adopt besides the mask a new precautionary measure in the form of a hood made of cloth with a square piece of silk (4 by 6 inches) sewed on in front to protect the respiratory entrance. This hood had two apertures for the eyes and was tucked inside the overall at the neck. With the exception of Dr. Yuan, none of our physicians or dressers, numbering over eighty, met with mishap.

EXPERIMENTS UPON SPUTUM OF PATIENTS

Many experiments were made upon the sputum of patients and dealt with the action of direct sunlight, indirect sunlight, drying under different conditions, sulphur fumes, formalin vapor, and over a dozen kinds of antiseptics and disinfectants upon the fresh sputum. A detailed list of our findings would consume too much time. Suffice it to say that in at least four samples of sputum exposed in bulk on a petri dish to the sun for two to six hours till they appeared dry to the naked eye we could still cultivate the *Bacillus pestis* by scraping the remainder.

With regard to fumigation we found that one average specimen of plague sputum placed in a petri dish in a room measuring 10 by

10 by 10 feet was more favorably acted upon by sulphur fumes than by formalin vapor. Out of seventeen observations made upon the former with exposures varying from four to twenty-four hours we could grow the *Bacillus pestis* on only one occasion (four hours). Out of twenty observations upon formalin vapor, we obtained cultures in eight cases (four to twenty-four hours). Light clothes and overalls, owing to their porous nature, were quickly sterilized by formalin vapor, hence formalin gas was generally used for overalls, alcohol for hands and gloves, while moist sulphur dioxide was employed for the fumigation of houses.

A large number of experiments have in the past been performed upon cultures of *Bacillus pestis*, but so far as we know this is the first time that a systematic attempt has been made to test the efficacy of antiseptics and disinfectants upon the actual plague sputum. The following experiments were made:

EFFECTS OF DISINFECTANTS UPON SPUTUM

Experiment A. Small cotton swabs mounted on iron wires were placed in test-tubes and sterilized by dry heat. Five cc. of fresh solutions of the antiseptic in different strengths were placed inside each tube. At the proper moment the swab was dipped into the sputum in a petri dish, suspended in the antiseptic solution for the requisite number of minutes, and then washed in sterile normal saline solution to remove excess of antiseptic. After this, the swab was introduced into a fresh agar tube and a culture made. The same procedure was repeated with the other solutions, care being taken to allow for as little discrepancy as possible in the quantity of sputum tested. The cultures were examined as a rule after forty-eight hours in the incubator kept at 30° C.

In this way 433 observations were made extending over a period of two months. The chemicals used were carbolic acid, mercuric perchloride, lysol, izal, phenol, potassium permanganate, hydrogen peroxide, lysoform, antiformin, rectified alcohol, methyl alcohol, lime-water, and slaked-lime. The time of immersion varied from one minute in the case of alcohol to thirty minutes in the case of antiseptic solutions. Our findings were rather surprising. For instance, in the case of carbolic acid, a solution of only 10 per cent for five

minutes was effective for preventing the growth of *Bacillus pestis*, in the case of mercuric perchloride only twenty minutes' immersion in 0.2 per cent solution, or thirty minutes in 0.1 per cent and 0.05 per cent solutions, was reliable; in the case of lysol (many brands used) twenty minutes' immersion in 2 per cent solution was necessary. Alcohol, either 90 per cent or undiluted, easily sterilized the sputum in three minutes; when diluted it was of no use. Both slaked-lime and lime-water were effective in thirty minutes. The other chemicals, including some much advertised specimens, appeared ineffective.

The viscosity of the sputum should, however, be taken into account when drawing any conclusion, but it may be wise for sanitary departments to consider these findings before launching into large purchases of so-called disinfectants for the control of plague epidemics.

EXPERIMENTS UPON TARABAGANS

Having failed to observe the existence of plague among marmots in the natural state, our next step was to ascertain how far such animals were susceptible to the *Bacillus pestis* under laboratory conditions. Like all rodents, the marmot, when inoculated subcutaneously or intraperitoneally with *Bacillus pestis*, developed septicemic plague, as has been shown by Strong, Kitasato, and myself. But I was anxious to observe the results of inhalation of the plague bacillus upon the animal. Dr. Strong conducted one such experiment at Mukden in 1911 upon two large tarabagans, and although both died, only one showed undoubted signs of primary lung infection. In 1916 Eberson and I continued these inhalation experiments upon the small marmot (*Spermophilus citillus*) found in large numbers around the graveyards of Mukden. A number of these animals received inhalation of *Bacillus pestis* ejected from a fine spray and were then thrown among others serving as contacts. The results were as follows (6):

First Series

Marmots inoculated	12	Deaths	8
Contacts	10	Deaths	3
Total	22	Total	11

Second Series

Marmots inoculated	7	Deaths	5
Contacts	9	Deaths	7
Total	16	Total	12

We could, therefore, reproduce conditions among small marmots similar to those observed among men, although the percentage of deaths among the animals (68.4 per cent of those who received inhalation and 52.6 per cent of contacts) might be higher than among human beings during epidemics.

In August, 1921, we commenced a series of experiments in Harbin upon the Mongolian marmot or tarabagan (*Arctomys bobac*) with a view to finding not only the susceptibility of this animal to plague pneumonia but also the existence, if any, of chronic or subacute plague among the species.

Experiment B. Tarabagan 1 was firmly strapped upon the prepared stage with the nose held inside an iron muzzle. It was then covered with an oblong metal box open at the bottom and having a small circular aperture at the top for the introduction of the nozzle of a spray.

A forty-eight hour agar slant culture of a virulent strain of *Bacillus pestis* from the 1921 epidemic was suspended in 10 cc. of salt solution and sprayed from a graduated cylinder fitted with a very fine nozzle. The technique is the same as in the Mukden experiments (6).

The same experiment was repeated upon Tarabagans 4, 7, and 10. Each animal so inoculated was kept with two healthy ones in a cage measuring 2 by 2 by 2 feet. Two cages had flea proof iron gauze partitions to prevent the possibility of flea complication. The operators took all antiplague precautions.

Experiment C. When Tarabagans 1, 4, and 10 died, eight healthy animals were introduced among the contacts, two into each cage, so that for the two experiments twenty animals were employed altogether. Rabbit controls were used in every case (Rabbits 1, 4, 7, and 10).

Experiment D. The same experiment as Experiment B was repeated with six tarabagans (Tarabagans 31 to 36), the first two

animals receiving direct inhalation from cultures obtained from dead Tarabagans 1 and 10 and the other four serving as contacts. All were placed in one cage $2\frac{1}{2}$ by 2 by 2 feet with no wire partition.

Results. All the six control rabbits died.

Rabbit 1	died	in	36	hours.	
Rabbit 4	"	"	40	"	
Rabbit 7	"	"	50	"	
Rabbit 10	"	"	50	"	
Rabbit 31	"	"	130	"	($5\frac{1}{2}$ days).
Rabbit 32	"	"	154	"	($6\frac{1}{2}$ ").

Of the marmots, Tarabagan 4 died in four and one-half days, showing at postmortem much inflammation of epiglottis and trachea, marked hemorrhages in left lung, peritoneum, and intestines. Tarabagan 10 died in five and one-half days showing at postmortem blood-stained froth from nose and mouth (as in man), congestion of trachea and bronchi, with a quantity of pink sputum and distinct hemorrhagic spots not unlike pneumonia in the lungs. Tarabagan 1 died seven and one-half days after inhalation and showed dark swollen cervical and bronchial glands, hyperemic trachea, and bronchi with pink sputum, and red patches of pneumonia in both lungs. Tarabagan 7 remained alive until the seventeenth day when it was killed with chloroform after a struggle of twenty minutes. At postmortem it showed swollen, dark cervical glands, slightly congested trachea, with semipurulent contents, many yellow patches in lung substance which on section proved to be abcesses. In the spleen, too, an abcess was observed at the anterior horn. The first three animals evidently died of plague pneumonia, while the fourth developed a subacute form of plague which did not seem to inconvenience it. Numerous plague bacilli were found in all animals except Tarabagan 7, where only a few scattered bacilli were seen in the heart's blood, peripheral blood, lung tissue, and cervical glands.

One contact which had been with Tarabagan 10 was also killed on the seventeenth day and showed no apparent lesions in the organs, but some plague bacilli detected in the heart's blood were confirmed by cultures later on.

Both of the animals that received direct inhalation in Experiment D died (Tarabagan 31 in five and one-half days and Tarabagan 32

in six and one-half days) and showed at necropsy changes similar to the others receiving inhalation in the other experiments.

The occurrence of plague bacilli, although few in numbers, in the blood of the two living tarabagans is of supreme importance, because it may explain the secret of the strange infections which have taken place in Siberia among Russians developing plague after skinning and eating apparently healthy animals. There are now under observation at Harbin still nineteen tarabagans which have been in contact with lung infected animals and their progress will be watched with interest.

POSTMORTEM RECORDS

Besides those at Hailar and Dalainor, we conducted forty-three complete postmortem examinations at Harbin, thirty-four of which were upon plague subjects, during the period from February 27 to May 21. Our findings will be related in detail before the Conference of Japanese Physicians at Port Arthur on September 24, but it may be interesting to note here that in the first part of the epidemic (before April 27) all cases except three babies were pneumonic. On that date one septicemic case was recorded, while during the two ensuing weeks all three necropsies done showed primary lung lesions. After May 13 every one of the ten postmortems performed was septicemic except one man who had a small patch of bronchopneumonia. From these pathological cases and our former clinical observations, it appears to us that the preponderance of the septicemic cases in the latter course of the epidemic exercised a marked influence upon its termination. If so, how was it effected? Could it be that the organisms passing through pneumonic cases were becoming so virulent that there was little or no time for the patients to develop pulmonary symptoms, and the medium of infection, namely the sputum, was therefore absent. As a consequence the later victims became less infectious, though invaded by more virulent bacilli, fewer infections took place, and the epidemic gradually died out. The alternative, namely, a diminished virulence of the organism on account of the warmer weather has little scientific evidence to support it; in our experiments conducted this summer the original strains grown in the winter seem to be as virulent as ever.

TREATMENT AND PROTECTIVE INOCULATION

The treatment of pneumonic plague, in this as in previous epidemics, proved exceedingly unsatisfactory and no authentic case is on record where any serum or medicine has saved life. In our hospitals, antiplague serum, neosalvarsan, eusol, formalin, sodium gynocardate, and methylene blue were tried but they were of no avail. No remedy has so far been found sufficiently powerful to stop the rapid distribution of the bacilli through the lungs and the blood.

While engaged upon the experiments dealing with the action of disinfectants upon sputum, we noticed on frequent occasions that when the cultures were contaminated with a spore-bearing bacillus plague organisms did not grow. This accident put into our heads the possibility of using the spore-bearing organism for protective inoculation. So this organism was isolated and found to be non-pathogenic and similar to the potato bacillus. The guinea pigs were next inoculated with emulsions of the pure cultures. In the stress of the moment, whole agar slants of virulent plague bacilli were then injected into the peritoneum of each of these guinea pigs. The first guinea pig died in two and one-half days, the second in five days, and the third in six days, whereas under ordinary circumstances such large doses would prove lethal in eighteen to twenty-four hours. Necropsy revealed in every case a localized peritoneal abscess with matting of the liver, spleen, omentum, and intestines, as if a strong local reaction had taken place. Under the microscope the pus showed besides the spore-bearing bacilli numerous plague bacilli, but the heart's blood showed only a few or none at all. Encouraged by these results, an emulsion of agar cultures of this spore-bearing bacillus, as well as a subtilis-like organism grown in large flasks, was injected into two plague patients, respectively, with however no apparent relief. The conditions, however, under which we were at that time working were not favorable, as our men were continuously threatened by the ignorant populace with personal violence and our hospital with fire. A well-fitted, glass-lined ward with a separate compartment where the operator could give intravenous injections might have been more satisfactory than the close, sparsely heated rooms where hundreds of patients had previously died.

While the above experiments are far from complete, we shall continue them with a view to discovering a virus, which while deadly to the parasite is harmless to the host, a process which has already been successfully used by the employment of rat-typhoid virus in combating plant parasites and in the extermination of plague-bearing rodents.

As is generally known to bacteriologists, the *Bacillus pestis* resembles morphologically the bacteria of a group classed under "hemorrhagic septicemia," whose other members produce highly fatal infectious diseases among lower animals. To this class of disorders belong especially the affections known as swine plague, fowl cholera, rabbit septicemia, and rinderpest. The bacilli are short, non-motile, non-spore-forming, Gram-negative with a tendency to bipolar staining. While the organisms of fowl cholera and swine plague are extremely fatal to their respective hosts, they are apparently quite harmless to man. Vice versa, the *Bacillus pestis*, so virulent to man, is absolutely innocuous to chickens, ducks, and pigs, as we have again proved by injecting even 5 cc. of human plague blood into a series of these animals, with negative results. Is it possible that our future hope of protection against pneumonic plague lies in these organisms of the same family? Or, shall we look to Koch's tubercle bacillus and allied bacilli for the solution?

May I make an appeal before closing this address? Through the generosity of Mr. Rockefeller, we have been enabled to witness the inauguration of this unrivalled home of medical training. The Rockefeller Foundation, by its marvellous organization, splendid resources, and true spirit, has conferred untold benefits upon a large part of the world. It has established this unique hospital and medical school in our midst. There are keen men of science in this as in other countries, who need only encouragement and opportunity to accomplish great deeds. At present, owing to incessant political strife and the general ignorance of modern science brought about by a non-progressive education based largely upon old classics, those undertaking research are seldom understood or appreciated. Is it too much to expect the Rockefeller Foundation to extend its beneficent activities and found in the insanitary yet glorious old land of China another

Rockefeller Institute, similar to but perhaps smaller in size than that in New York, where the historic work of Welch, Flexner, Noguchi, Heiser, and Carrel may be duplicated in such diseases as leprosy, beri-beri, malaria, tuberculosis, intestinal parasitism, plague, sprue, trachoma, malignant scarlatina, and other affections peculiar to the East? As one who has been fighting for the right to work during the last fourteen years, I earnestly hope that the Trustees of this, the greatest individual charitable organization in the world's history, may seriously consider it.

SUMMARY

1. Pneumonic plague epidemics arise as a secondary manifestation of bubonic plague.

2. The prevalence of purely septicemic cases towards the end of the epidemic is significant as a probable explanation of its decline and termination.

3. Subacute or chronic plague may exist among the tarabagans in Mongolia and Siberia, giving rise to periodic outbreaks of bubonic plague in man, as a result of direct infection from injury due to skinning by trappers or marmot eaters.

4. The tarabagan is easily susceptible to pneumonic plague produced by inhalation of the *Bacillus pestis* in spray form.

5. The existence of pneumonic plague carriers was proved in the 1921 Manchurian epidemic.

6. Rooms where patients have died of pneumonic plague are not particularly dangerous. In all four instances recorded, sick patients travelling in railway cars have not infected their fellow passengers.

7. Disinfectants and antiseptics even in strengths above those usually employed have very little effect upon plague sputum. The use of alcohol is the surest means of sterilizing the hands and gloves in plague work.

8. We have cultivated plague bacilli from the seemingly dry sputum of patients.

9. The mask is the principal means of personal protection against pneumonic plague.

10. The problem of successful vaccination against pneumonic plague still awaits solution.

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THE CLINICAL IMPORTANCE OF THE VITAL CAPACITY OF THE LUNGS

By

Francis W. Peabody, M.D.

INTRODUCTION

In *The Doctor's Dilemma* Bernard Shaw makes old Sir Patrick Cullen tell his young colleague, flushed with pride at a new discovery, that "most discoveries are made regularly every fifteen years." This cynical questioning of all progress in medicine is unwelcome to us, but there is much truth in the fact that the younger generations, walking by different lights and along apparently new paths, find themselves facing the very problems that confronted their fathers and very little better equipped to solve them. The vital capacity of the lungs, or the volume of the deepest expiration after the greatest possible inspiration, was the subject of a brilliant and painstaking investigation seventy-five years ago, in which its physiological significance was discussed and its bearing on clinical medicine indicated. After receiving a considerable amount of attention, chiefly on account of its practical interest, the subject faded into the background and was lost sight of by clinicians, but within the last few years it has again begun to assume an importance in medicine.

EARLY WORK

In 1846, John Hutchinson (1) published his paper, "On the Capacity of the Lungs and on the Respiratory Functions, with a View of Establishing a Precise and Easy Method of Detecting Disease by the Spirometer." Like so many of the articles by the older school of English physicians it has achieved the position of a classic and all that has been since added to the subject is development of detail, almost in the nature of ornamentation. Hutchinson was not the first to attempt to determine the vital capacity of the lungs for in his careful survey of the literature he mentions a number of earlier investigators, but all of them used crude methods and made few observations, whereas, as Hutchinson says, this is the

type of investigation which "demands for its solution a multitude of experiments, almost without limitation." The care which he took to fulfill its critical requirements is illustrated by the fact that he examined 2,130 persons of different types, including sailors, paupers, Royal Horse Guards, Woolwich Marines, draymen, girls, and even gentlemen. Hutchinson was the first to realize that the magnitude of the capacity of the lungs depends on other bodily functions and to attempt to determine with what function it was most closely related. He also appreciated fully the effect of disease on the vital capacity and gave striking illustrations of the value of determinations of the vital capacity of the lungs in diagnosis and prognosis of pulmonary tuberculosis. And finally, it was Hutchinson who made the method available for general use by devising a simple and accurate spirometer, the form of which has not been substantially altered.

John Hutchinson saw from the outset that the importance of spirometry as an aid to the clinician depends largely upon the possibility of establishing reliable normal standards, deviation from which would indicate a pathological condition. For this reason, in sad contrast to much present-day so-called scientific work, he devoted by far the greater part of his attention to the study of what we should call the "normal control." His conclusions were that the three factors having the most marked effect on the vital capacity of the lungs are weight, height, and age. Height was found to have the greatest influence and he says that "for every inch of height (from 5 feet to 6 feet) 8 additional cubic inches of air, at 60°, are given out by a forced expiration." The effect of weight was found to be more irregular than that of height, and, unless there is abnormal obesity, it is overwhelmed by that of height. Age appeared to have less influence than height or weight but Hutchinson states that the vital capacity increases from fifteen to thirty-five years and decreases from thirty-five to sixty-five years. The circumference of the chest, the length of the trunk, and the size of the chest as determined by plaster casts were studied and seemed to have little effect, but slight changes in the vital capacity due to posture were described. Many investigators since the time of Hutchinson have applied themselves to the attempt to find more reliable normal standards. Wintrich (2) (1854) made determinations on 3,500 normals and

states that height, age, and sex are the chief factors of importance. The influence of old age is shown mainly after 50 for the figures between forty and fifty differ little from the minimum values for the age period of twenty to forty. He mentions as other factors, (1) the effect of eating and drinking in raising the diaphragm, (2) constipation, and especially (3) a rapid respiratory rate, which may prevent the taking of a deep breath, but he found that pregnancy exerts little influence on the vital capacity. Arnold (3) (1855) made a similar extensive study and attempted to estimate the effect of age, sex, size, expansion of chest, and habits of life on the vital capacity. Waldenburg (4) (1875) agreed essentially with Arnold but found the quantitative effect of height to be slightly different. He also cites Müller (1868) who described a lung capacity quotient which varies directly with the square of the chest circumference and the length of the trunk and he believes this to be the best basis for comparison. Waldenburg, as well as other earlier authors, lays special stress on the fact that under given circumstances the vital capacity of any individual remains extremely constant. In 1918, Lundsgaard and Van Slyke (5) correlated the vital capacity of the lungs with the chest volume as calculated from three easily obtainable measurements of the thorax, but the number of individuals studied was only eighteen, and in a larger series West (6) subsequently found that the method offered no advantages.

RECENT INVESTIGATIONS

The factors already mentioned remained the chief ones with which it was attempted to correlate the vital capacity of the lungs until quite recently when it became apparent that certain physiological functions, such as the basal metabolism, bear a very close relationship to the area of the body surface. In 1917, Peabody and Wentworth (7) suggested that vital capacity might vary more closely with surface area than with the factors hitherto employed and a small number of observations seemed to bear this out. In 1919, Professor Dreyer (8) of Oxford published very complete observations on nineteen normal persons and concluded that the relation between surface area and vital capacity is constant, but that the value of K will vary for groups of individuals whose nature of life

and habits are distinctly different. Finally, in 1920, West (6) studied 129 normals at the Peter Bent Brigham Hospital (eighty-five men and forty-four women) and again showed that the vital capacity varies more uniformly with surface area than with any other function. West found for men an approximate standard value of 2.5 liters vital capacity per square meter of body surface and for women a value of 2.0 liters per square meter. The area of body surface is readily determined from the height and weight by means of the chart of Du Bois and Du Bois (9) so that in West's calculations the three great determining factors of height, weight, and sex are accounted for. It is interesting and satisfactory that the calculation of West's figures by means of the formula of Dreyer showed practically complete agreement, so that it is unimportant whether one expresses results in percentage of normal, according to West, or as a variation of a constant, according to Dreyer. Of West's subjects 71 per cent had a vital capacity within 10 per cent of the normal standards and only 5.5 per cent had a vital capacity more than 10 per cent below the normal standard. As will subsequently be seen, it is the decrease below normal standards that is of significance in pathological conditions.

At the present time there is no doubt that the most reliable standards on which to base abnormal deviations of the vital capacity of the lungs in disease are those of Dreyer (8) and West (6), which take into consideration sex and body surface area. Our knowledge of this fundamental aspect of the subject is, nevertheless, still very incomplete. Much remains to be learned about the variations of these standards with age for the results of both Dreyer and West deal almost exclusively with young adults. Infinitely more baffling are the effects on the vital capacity of different habits of life. Physical exercise and athletic training tend to increase the vital capacity, while a sedentary existence exerts its influence in the opposite direction, but the effects do not appear to be constant and it is doubtful whether they can ever be satisfactorily expressed quantitatively. As in many other bodily functions, such as pulse rate, respiration rate, and even temperature, one must accept the fact that there will always be certain individual variations from general standards of normality. It is important to appreciate, how-

ever, that this does not detract essentially from the value of such normal standards. It merely indicates that individual findings should be interpreted with judgment and in the light of broad experience, in exactly the same way that it is necessary to interpret many other findings in clinical medicine, and it illustrates the general importance of a knowledge of this as of other functions in any individual while in a normal state.

VALUE OF SPIROMETRY

Before referring to the alterations in the vital capacity of the lungs which occur in different specific diseases, it will be well to consider the fundamental physiological significance of such alterations, and to make clear the general type of information that may be obtained by means of spirometry. A decrease in the vital capacity occurs in many clinical conditions, but it is not of direct or specific diagnostic moment. The determination of the vital capacity is to be regarded purely as an index of the functional capacity of one part of the respiratory mechanism and particularly as a means of obtaining information as to a diminution of its normal reserve power. Just as the phenolsulphonethalein test gives information regarding some, but not all, of the functions of the kidney, so the determination of the vital capacity gives an insight into one function of the lungs. The physiological activities of the external respiration may be broadly grouped into two categories; those which are related to the pulmonary movements, the expansion and collapse of the lungs, and those which have to do with the respiratory membrane. As a respiratory membrane, the function of the lungs is essentially to promote the interchange of gases between the blood and the air in the alveoli, and this has only an indirect relationship to the vital capacity. The movement of the lungs, on the other hand, by which the ventilation of the alveoli is brought about, is very directly dependent on the vital capacity because it is this factor that largely determines the extent of the expansibility of the lungs and thus the possible extent of the pulmonary ventilation. The practical importance of the adaptability of pulmonary movements to bodily needs is self-evident, for an increase in pulmonary ventilation almost necessarily accompanies any increase in metabolism

whether this be due to exercise, to fever, or to some other stimulant such as that associated with hyperthyroidism. When a man lies quietly at rest his bodily activities are nearly at a minimum and his total metabolism is approximately what we regard as "basal." In this state his oxygen requirements are small and the necessary amount of oxygen is easily supplied to the arterial blood by slow and rather shallow breathing. The minute-volume of pulmonary ventilation is low. With any increase in muscular activity the organism will require more oxygen and the absorption of this additional oxygen, as well, of course, as the elimination of increased amounts of carbon dioxide formed, is accompanied by an augmentation of the minute-volume of air which is brought into contact with the blood in the capillaries of the lungs. The minute-volume of air breathed increases with the metabolism but in general at a slightly less rapid rate than the latter. This rise in minute-volume is brought about by increasing both the rate and depth of breathing. Practically, however, on account of the fact that with each respiration a certain proportion of the inspired air remains in the upper respiratory tract or "dead space" and thus takes no part in gaseous exchange, it is much more economical to take deep and slow respirations than to take shallow and rapid respirations. With deep breathing the ventilation of the alveoli of the lungs, where gaseous interchange takes place, is brought about with a lower total ventilation than with shallow breathing. The highest minute-volume that any individual is capable of maintaining in response to the requirements of his metabolism will depend on his ability to increase the rate and depth of breathing and on the balance between rate and depth. Practically, a healthy young man who is carrying on extremely hard exercise breathes about ten times as large a volume of air as he does when at complete rest. This difference between the minute-volume of air breathed at rest and the highest minute-volume that can be maintained represents what may be called the "pulmonary reserve" — the reserve power of the external respiratory mechanism to be called upon in time of need. The pulmonary reserve depends on rate and depth of breathing, but of these two factors the ability to increase rate is at the same time the least important and the least affected by pathological conditions. The rate at which the

respiration can be carried on effectively and continuously is somewhat definitely limited and even with hard exercise it is unusual to find rates much above 35 per minute. The more important factor, therefore, in increasing the minute-volume of air breathed is the depth of breathing, and, as a corollary to this, it is evident that the limits to which the minute-volume can be increased and to which the pulmonary mechanism can be adjusted to the needs of the body will depend very largely upon the ability to increase the depth of the respiration. It is here that the vital capacity becomes the prominent determining factor, for the ability to breathe deeply depends very largely on the vital capacity of the lungs. It is obviously impossible to use the total volume of the vital capacity for continuous respiration and even under the most favorable circumstances only a comparatively small proportion is available. In a series of normal young men who rode a stationary bicycle until they were forced to stop on account of dyspnea, it was found that at the end, when the minute-volume was greatest, they were using on the average about one-third of their vital capacity at each respiration. Roughly, therefore, one may say that a normal man with a vital capacity of 4,500 cc. will breathe 400 cc. per respiration while he is quietly at rest and that with his maximum requirement it is possible for him to breathe about four times as much, or 1,600 cc. per respiration.

If, however, owing to some pathological condition, his vital capacity is reduced 50 per cent to 2,000 cc., the same subject will be able to increase the depth of his respiration only from 400 cc. at rest to 700 cc. when he is exercising. With a rate of respiration of 35 per minute he would be able to keep up a minute-volume of 56 liters in the first instance but of only 25 liters in the second. Whereas in his normal state he could theoretically carry on his metabolism at about ten times its normal level so that he could run a race, his condition when his vital capacity was reduced would be such that he could meet only a fivefold increase in metabolism and would become short of breath walking rapidly upstairs. The decrease in vital capacity may thus give a fairly accurate indication of the amount of physical activity which can be undertaken without the production of dyspnea. The determination of the vital capacity will instruct us as to the functional capacity of the external respiration for it will serve as an index of the respiratory reserve.

EFFECT OF DECREASE IN VITAL CAPACITY

An actual experiment, illustrated on the accompanying table, indicates the effect of a decrease in the vital capacity of the lungs on the respiratory mechanism and the production of dyspnea. The subject was a normal medical student and the reduction of the vital capacity was produced by the use of a tight chest swathe which restricted the movements of the thorax.

In spite of the artificiality of the procedure it will serve a purpose for it demonstrates the simple mechanical effect of a decrease in vital capacity on the production of dyspnea, and is not complicated by the numerous other factors which are present in most pathological conditions. On the whole, it gives a fairly accurate representation of the picture in a pleural effusion in which dyspnea rests largely on a mechanical basis. In Experiment A, the subject has a normal vital capacity of 4,200 cc. If, as has been stated, a normal person carrying on extremely hard exercise breathes at a rate of about 35 per minute, and uses approximately one-third of his vital capacity at each respiration, then one may calculate the maximum minute-volume possible for this subject as 49 liters $\left(\frac{\text{V.C.}}{3} \times 35 = 49 \text{ liters}\right)$. In Period 1, at complete rest, his minute-volume is 4.2 liters, or only 9 per cent of his possible maximum. In Period 2, he walked upstairs on a treadmill at a constant rate for one minute and the minute-volume rose to 12.9 liters. In this, as in all other similar observations, it has been found that the dyspnea noticed by the subject is greater in the first minute after walking than during the exercise itself. In Period 3, after the walk, the minute-volume has risen to 15.0 liters, or 31 per cent of the maximum minute-volume. With this minute-volume the subject was conscious of breathing somewhat deeply but was not at all short of breath. In Period 4, he repeated exactly the walk in Period 2 but carried a pack weighing 50 pounds on his back. The minute-volume rose to 17.8 liters, and in the first minute after (Period 5) it was 23.8 liters, or 49 per cent of his maximum minute-volume. During this period (Period 5) the subject was slightly dyspneic. The increase in minute-volume is obtained by increasing the rate of respiration to 20, and increasing the volume per respiration from 320 to 1,190 cc. In Period 5, the volume of each respiration

Experiment to Illustrate the Effect of Reduction of the Vital Capacity of the Lungs on the Production of Dyspnea

	Experiment A Vital Capacity; Normal = 4,200 cc. Maximum Minute-Volume = $\frac{V.C.}{3} \times 35 = 49$ liters					Experiment B Vital Capacity; Reduced = 2,800 cc. Maximum Minute-Volume = $\frac{V.C.}{3} \times 35 = 33$ liters				
Period	Rate	Volume per Respiration cc.	Per cent of Vital Capacity	Minute-Volume Liters	Per cent of Maximum Minute-Volume	Rate	Volume per Respiration cc.	Per cent of Vital Capacity	Minute-Volume Liters	Per cent of Maximum Minute-Volume
1. Rest	13	320	8	4.2	9	18	310	9	5.6	17
2. Walk up-stairs	22	590	14	12.9	26	26	670	24	17.5	53
3. Rest 1st minute	15	1,000	24	15.0	31 No dyspnea	28	764	27	21.4	65 Moderate dyspnea
4. Walk up-stairs with load	24	740	18	17.8	36	33	700	25	23.1	70
5. Rest 1st minute	20	1,190	28	23.8	49 Slight dyspnea	32	778	28	24.9	75 Marked dyspnea

is 28 per cent of the vital capacity of the lungs, but the rate of respiration is comparatively slow and the subject has little difficulty in maintaining the necessary minute-volume. In Experiment B, the same observations were made on the subject after his vital capacity had been reduced to 2,800 cc. by a chest swathe. At this time the theoretical approximate maximum minute-volume is only 33.0 liters because of the decrease in vital capacity. In Period 3, after the first walk, the minute-volume was 21.4 liters, or 65 per cent of the maximum minute-volume, and the subject noted much more dyspnea than during Period 5 in Experiment A. In Period 5 (Experiment B), the minute-volume was 24.9 liters, or 75 per cent of the maximum, and the dyspnea was great. It will be seen that in this experiment, as in Experiment A, the subject increases the depth of respiration until it is about 28 per cent of his vital capacity, but this is so low in Experiment B (778 cc.) that it becomes necessary to increase the rate in order to maintain the minute-volume necessary to supply the oxygen required by the high metabolism. In Period 5 the rate reaches nearly the highest that one expects to find during severe exercise. By comparing the figures which indicate the percentage of the maximum minute-volume which is being used it will be seen that as this percentage rises the feeling of dyspnea increases progressively so that with 50 per cent the dyspnea is slight, but with 75 per cent it is very marked. The amount of work done in Period 4 was the same in both experiments, but in Experiment B much more dyspnea was produced than in Experiment A. In Experiment B the vital capacity was low and the subject could not breathe as deeply as in Experiment A, so it became necessary for him to increase the rate of respiration. The values for minute-volumes are higher for the corresponding periods in Experiment B than in Experiment A and this is due to increased rate and relative increase in "dead-space," but for the sake of simplicity these points will not be discussed. The important point to be observed from the experiments is that the inability to increase the depth of respiration is the factor which reduces the pulmonary reserve in Experiment B and causes the production of dyspnea. This inability to breathe deeply, depends on the vital capacity of the lungs, and thus the vital capacity is an important factor in determining the occurrence of dyspnea. Indeed,

if one knows the degree to which the vital capacity is decreased it is possible to calculate with a fair degree of accuracy the maximum minute-volume which a patient can maintain and thus foretell how much physical exercise he is capable of without undue shortness of breath.

What has been said so far should not, of course, be taken to suggest that changes in the vital capacity of the lungs are the only factors in the production of dyspnea. This is obviously far from being the case. Even among normal individuals with vital capacities of equal size there is a wide variation in the tendency to dyspnea. Physical training and the development of skeletal muscle determine the ability to keep up continuously a high pulmonary ventilation without fatigue, while the character of the heart muscle, the rate of circulation, the morphological and chemical constitution of the blood, and the state of the respiratory membrane are merely a few of the other factors which may affect the delivery of oxygen to the tissues and the removal of carbon dioxide, and thus play a rôle in the production of dyspnea. Nevertheless, in certain pathological conditions dyspnea is due very largely to an inability to increase the ventilation of the lungs, and it is important, as well as interesting, to the clinician that this decrease in the reserve power of a vital function can be followed in a quantitative way by means of spirometry.

VITAL CAPACITY IN RELATION TO DISEASE

Having discussed in some detail the general significance of the vital capacity of the lungs, we may now turn to a consideration of the subject in its relation to disease. There are many conditions which may cause a decrease in the vital capacity. Anything which interferes with the respiratory movements of the thorax may do it; for example, extreme general muscular weakness (as after prolonged infections), calcification of costal cartilages, arthritis and similar conditions affecting the mobility of the ribs, as well as intra-abdominal conditions which inhibit the descent of the diaphragm. Pleural effusion or pleural pain may act in the same way. Inflammatory and infiltrative lesions affecting the lung substance, such as pneumonia, tuberculosis, and carcinoma, decrease the vital capacity by obliteration of air spaces as well as by interference with lung mobility. In

emphysema an alteration of the elasticity of the lung, associated with inability to collapse, decreases the vital capacity. In heart disease still another element enters in and the lowering of the vital capacity depends on increased pressure in the pulmonary circulation and engorgement of the pulmonary vessels. Finally, of course, in any given case several of these factors may be operative at the same time, so that in a severely decompensated cardiac patient the low vital capacity may be due to circulatory disturbances, pleural effusion, pulmonary infarct, and a superimposed bronchitis.

If, therefore, the situation is so complex, and such a variety of causes may bring about changes in the vital capacity of the lungs, one may well ask what it is that spirometry has to offer to the clinician. It is quite evident that it offers nothing of a specific diagnostic nature. Like many other clinical methods, such as the determination of the temperature, the leucocyte count, the presence of albumin in the urine, or the gastric acidity, it merely indicates a general type of process and leaves it to the observer to discover the underlying cause and to interpret its significance. But the determination of the vital capacity goes a little further, for it gives, within certain limits, an idea of the extent of the process. It has a quantitative value. It shows that the function of pulmonary ventilation is affected, and it indicates the degree of the pathological condition. It supplements the history, physical examination, and X-ray examinations by giving additional information as to the functional capacity of the lungs. It may also indirectly indicate the extent of anatomical involvement of the lungs; for in many cases of tuberculosis or cancer, for instance, the vital capacity test indicates an involvement much greater than is suggested by the physical signs and one that is more in harmony with the X-ray and autopsy findings. Sometimes, indeed, as in two cases of metastatic carcinoma of the lung recently observed, the changes in vital capacity appear to follow the progress of the disease even more accurately than the X-ray pictures. As a functional test, it gives an indication of the pulmonary reserve, and in heart disease enables one to tell, while the patient is still in bed, just about how much physical activity he is capable of without developing dyspnea. The determination of the vital capacity at intervals of time gives much information as to the course of the

disease, and, as it is a quantitative method, it can be used for graphic expression. Spirometry may also serve as a valuable check on the history, especially as regards the history of dyspnea, which may be either understated or exaggerated. Thus, a patient with heart disease who says he has no dyspnea on exertion may be found to have a low vital capacity, and it is discovered that the absence of this symptom is due to the very limited life he leads. Or a patient who complains of great dyspnea on exertion is found to have a normal vital capacity and the suggestion is clear that the symptom is due, not to organic disease, but to some nervous factor in his condition. This point has often been of assistance in differentiating cases of so-called "effort syndrome" in which the physical examination suggested the possibility that the dyspnea might be due to early cardiac disease.

There are certain definite limitations to the clinical use of spirometry. The most important of these is the unwillingness or inability of certain persons to co-operate to the full extent of their ability. The test is not wholly objective and it is worthless unless the subject co-operates completely. This difficulty is met with in patients who do not understand what is desired, in very sick patients, and in certain highly neurotic individuals. The second important limitation to the value of spirometry is the comparatively wide normal variation from the average standards. This may be in some degree obviated by the development of better standards but at present the changes from time to time in any individual case are of more value than are the relative deviations from the normal standards. For practical purposes it may be assumed that normal young adults have a vital capacity of at least 90 per cent of the normal standards, but it must be remembered that this is a general figure and a few normals will fall a little lower. Still greater deviation must be allowed for subjects over fifty years of age until satisfactory standards have been established for the decades from fifty to seventy years. The question of the effect of general weakness must also be considered when determinations are made on persons who have been sick for a long time. The fact, however, that patients with pernicious anemia, a disease with a prolonged course in which general weakness is a prominent feature, usually have a vital capacity of more than 80 per cent of the

normal shows that, except in extreme cases, general weakness is not important (Peabody and Sturgis (10)). Fatigue or weakness of the muscles of respiration appears to be a less important factor than might be expected. This is indicated also by observations on a group of patients with heart disease in whom the vital capacity was low. An attempt was made to tire out the muscles of respiration by taking the vital capacity every fifteen seconds for ten minutes, but at the end of the forty observations the vital capacity was just as high as at the beginning.

SPIROMETRY AS A TEST OF PHYSICAL FITNESS

Practical interest in spirometry has recently been shown in two directions. It has been investigated in its relation to disease, and as a test of general physical fitness. The need for the tests of physical fitness developed during the war, and Professor Dreyer of Oxford suggested the determination of the vital capacity of the lungs as an objective method of classifying soldiers according to their physical condition. This phase of the subject, however, I shall not touch upon.

Heald and Thomson (11) recognized the value of Dreyer's test and combined it with the respiratory tests of Flack in such a way that they feel they have developed a much more accurate method of discriminating between men who are fit and those who are unfit. Observations on a similar group of men were made by Levine and Wilson (12), who studied 131 British soldiers with "irritable heart." They found that the average vital capacity was slightly decreased and corresponded with the general physical condition but that only in the group classified as "permanently unfit" was it more than 10 per cent below the normal standard. This is in agreement with the results of Adams and Sturgis (13), who examined 100 American soldiers with so-called "irritable heart" and found that only twenty had a vital capacity less than 90 per cent of normal. The decrease in vital capacity was not sufficient to explain the degree of dyspnea complained of. It is interesting that Levine and Wilson found a greater fall in vital capacity after exercise in the men who were unfit than in those who were fit. White (14) also made use of the vital capacity and the respiratory tests of Flack in estimating the physi-

cal fitness of soldiers. His subjects included normals, convalescents from acute infections and from "gassing," "effort syndrome" cases, and neurotics with "shell shock." The values for the vital capacity and the other respiratory tests were very low in the "shell shock" cases. White, therefore, concluded that in the groups under discussion the vital capacity is a test of nervous stability rather than of the condition of the cardiovascular or respiratory systems *per se*. The extraordinary tendency to fatigue in soldiers with "shell shock" and in cases of severe "effort syndrome," as well as in the neurasthenics of civil life, is quite definitely due more to weakness of will than to weakness of muscle. In all such cases any test involving effort or concentration will undoubtedly be of little value except as an indication of nervous stability. Where the will is weak the volume of air expired will be low, and lower than can be accounted for by muscular weakness, but the readings on the spirometer must not be taken as indicating any organic disturbance of the respiration.

VITAL CAPACITY IN RELATION TO PULMONARY TUBERCULOSIS

Of the diseases in which the vital capacity of the lungs has been studied pulmonary tuberculosis has received the most attention. Hutchinson (1), in 1846, placed much emphasis on the significance of spirometry in the early diagnosis of phthisis and gives an interesting account of his experience with Freeman, the American prize-fighter, then visiting England. At the first observation, in 1842, he was found to have a high vital capacity of 434 cu. in., but two years later it had fallen to 344 cu. in. At this time he was in ill health, but two physicians could find no evidence of pulmonary disease by auscultation. Freeman subsequently died, however, and at autopsy an extensive tuberculosis of the lungs was found. Wintrich, Arnold, and others also believed the method to have diagnostic value, and the former considered that the vital capacity was of aid in prognosis. Low values in phthisis were later reported by many investigators. In 1918, Garvin, Lundsgaard, and Van Slyke (15), using normal standards based on the chest volume, found a slight decrease in incipient cases and a considerable decrease in advanced cases of pulmonary tuberculosis. But the development of other improved methods for studying tuberculosis relegated spirometry completely

into the background until in 1920 Dreyer and Burrell (16), attacking the subject with better normal standards, again advocated its use. As a result of their study of a considerable series of cases they concluded that it is of value in the classification of patients in that this can be done on the basis of a numerical value instead of as the result of personal interpretation of physical signs, and that it is particularly helpful in following the course of the disease and the effects of the treatment. These results have since been confirmed in the United States by Wittich, Myers, and Jennings (17), who investigated 174 cases of pulmonary tuberculosis and again found a close correlation between the vital capacity and the clinical condition of the patients. In arrested cases the vital capacity was very near the normal value. Scattered observations have been made on the vital capacity in other pulmonary conditions such as acute bronchitis, emphysema (Wintrich (2), Peabody and Wentworth (7), Hoover (18), Siebeck (19)), asthma (Wintrich, Peabody and Wentworth), pneumonia (Wittich, Myers, and Jennings (17)), pneumothorax (Means and Balboni (20)), and pleural effusion (Pick (21), Peabody and Wentworth (7)), but no comprehensive studies have as yet been made. In this connection it is of interest that Graham (22) has shown that the vital capacity is also of importance to the surgeon in the operative treatment of empyema, for, used in connection with a mathematical formula devised by him, it will indicate approximately the maximum opening in the chest wall compatible with life if the mediastinum is not stabilized by adhesions.

VITAL CAPACITY AND HEART DISEASE

With the close relationship which exists between the vital capacity of the lungs and the production of dyspnea, it is rather curious that so little attention has been paid to spirometry in the clinical condition in which dyspnea is the most prominent symptom. In heart disease dyspnea is perhaps the commonest symptom, and the degree of dyspnea or the tendency to dyspnea has always been regarded as a rough index of the severity of the case and the degree of circulatory failure. If the vital capacity of the lungs is an expression of the tendency to dyspnea, as has already been shown, then it is apparent that the vital capacity may also serve as an index of the

clinical condition in patients with heart disease. Many observers (Arnold (3), Rubow (23), Bittorf and Forschbach (24), Siebeck (19)) have shown that the vital capacity may be decreased in heart disease, but it is only within the last few years that the subject has been carefully studied at the Peter Bent Brigham Hospital and an attempt made to correlate the vital capacity with the clinical condition. Briefly, the observations on a large number of patients have shown that in the early stages of cardiac disease, when there is no evidence of circulatory insufficiency, the vital capacity is within normal limits. As the condition progresses and the cardiac reserve becomes encroached upon so that physical exertion produces undue dyspnea, the vital capacity decreases and the diminution in vital capacity parallels very closely the development of the disease. If the vital capacity is below 40 per cent of the normal the patients are greatly limited and are practically bed-ridden. With a vital capacity above 40 per cent of the normal patients can usually be out of bed but unless the vital capacity is over 50 per cent they are severely handicapped, and even with a vital capacity of 60 to 70 per cent they can rarely expect to lead anything but a very quiet life. With a vital capacity of 70 to 90 per cent patients can often carry on a normal existence limited by the fact that any unusual exertion produces dyspnea. The determination of the vital capacity gives a good indication of what one may expect a patient to be able to do and the information may be obtained while the subject is remaining quietly in bed. Its chief value, however, is in following the course of the disease and as a guide to treatment. In ambulatory cases of heart disease the physical examination usually alters very little over long periods of time and opinion as to the course of the disease must then be based largely on the patient's recital of his symptoms. The most important of these is the tendency to dyspnea and in the vital capacity one has a quantitative method of following the development of this symptom. Changes in the vital capacity may occur without any objective evidence of cardiac insufficiency such as pulmonary edema, tender liver, or swelling of the ankles. It may thus be an early indication for active treatment. In severely decompensated cases, such as one finds in a general hospital, the vital capacity is very low, but with satisfactory treatment it will rise

quickly. West and Pratt (25) have shown the value of spirometry in following cases after the administration of digitalis. It is of particular interest in cases with a regular cardiac rhythm in which there is little effect on the heart rate, for the alterations in vital capacity are one of the best indices of the effect of digitalis in promoting clinical improvement. Charts on which the vital capacity is plotted from day to day give an excellent graphic record of the course of the disease. With improvement in the circulatory condition, the vital capacity rises; if the situation becomes worse, it falls; and if the condition remains stationary, the vital capacity does not change. Thus, after days or weeks of treatment one has a graphic record of the course of the case which is of distinct aid in prognosis, and which gives more definite information as to the functional condition of the patient than do any of the other records which are customarily kept.

In the later stages of heart disease it is easy to see what may cause a reduction in the vital capacity of the lungs. General physical condition, pulmonary edema, pleural effusion, hepatic enlargement, and analogous conditions will all effect the movability of the lungs, but the decrease in the early stages, before any physical signs develop, is less easy to understand. Many years ago Professor von Basch of Vienna suggested that cardiac dyspnea is due to "Lungenstarrheit," or pulmonary rigidity resulting from congestion of the pulmonary vessels, and last winter Professor Drinker, Dr. Blumgart, and I were able to prove experimentally (26) that engorgement of the pulmonary circulation interferes with the entrance of the air into the lungs. The experimental conditions simulated so closely those which obtain in certain types of heart disease that the results can be safely interpreted as explaining the clinical findings, and it seems clear that the important factor underlying the decrease of the vital capacity of the lungs in early cases of cardiac disease is the circulatory disturbance. It is thus evident that observations on the vital capacity give us an insight into the condition of the pulmonary circulation. The practical significance of this is obvious, for in most cases of heart disease the earliest symptoms of circulatory failure are referred to the respiration and suggest disturbances in the pulmonary circuit, dyspnea precedes peripheral edema. Thus we have in the determination of the vital capacity of the lungs a means of

obtaining information about this fundamentally important area of the circulation which cannot be obtained in any other way.

CONCLUSION

Such, then, briefly sketched, is the present relation of spirometry to clinical medicine. The development of more modern methods for the study of disease has resulted in the overshadowing of what was once regarded as a useful aid to diagnosis and prognosis, but none of the newer procedures gives the same type of information as is obtained from observations on the vital capacity of the lungs. With the general interest now manifested in the disturbances of physiological functions in disease, it is probable that the mechanism of the external respiration will receive its share of attention, and as an index of the ventilatory function of the lungs, the determination of the vital capacity will be of much value.

Recent investigations have brought out somewhat improved normal standards with which to compare the variations of the vital capacity in disease; they have broadened the clinical application of the method and have increased our understanding of the physiological significance of the vital capacity of the lungs, but the fundamental work of John Hutchinson has stood the test of time. It is a model exposition of scientific work, and the concluding sentences, which indicate the greatness of the author, might well serve as a text for all investigators. "The matter of this communication," he says, "is founded upon a vast number of facts — immutable truths which are infinitely beyond my comprehension. The deductions, however, which I have ventured to draw therefrom, I wish to advance with modesty, because time, with its mutations, may so unfold science as to crush these deductions, and demonstrate them as unsound. Nevertheless, the facts themselves can never alter, nor deviate in their bearings upon respiration — one of the most important functions in the animal economy."

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THE ORIGIN OF BLOOD-CELLS*

By

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INTRODUCTION

In 1920, the writer published an account of a study of the origin of the vascular system as it can be made out by watching the living chick blastoderm of the second day of incubation. The method of the origin of vessels can be made out in such specimens, in the area pellucida of the yolk-sac, in stages which range from the time just before the first somite through the stage of about twenty somites.

In the area pellucida there are three well-known layers, the ectoderm, the double layer of the mesoderm lining the extra-embryonal cœlom, and the endoderm. The blastoderms are mounted in a hanging drop preparation, in Locke-Lewis solution, with the endoderm against the cover-slip. The area pellucida is so thin that the endoderm, the vascular zone between the endoderm and mesoderm, and the mesoderm can all be analyzed with an oil immersion lens. The technique was described in 1920 (1).

BLOOD-VESSELS

Blood-vessels begin by the differentiation of a new type of cell from mesoderm. This cell moves out of the mesoderm, develops a dense, basophilic, azurophilic cytoplasm and becomes physically more refractile than mesoderm. As soon as this cell divides, it shows its essential characteristics, namely, the tendency of the cells to stay together to form syncytial masses. These masses of cells put out sprouts by which they join similar masses to form a plexus. While such solid clumps are still isolated, and after the plexus is formed, the cells become transformed into vessels by a liquefaction of the central part of the mass to form blood-plasma, while the periphery differentiates into endothelium.

* This paper was subsequently published under the title of, "Studies on blood: the vitally stainable granules as a specific criterion for erythroblasts and the differentiation of the three strains of the white blood-cells as seen in the living chick's yolk-sac." Johns Hopkins Hosp. Bull., 1921, xxxii, 314.

Dissecting Room, Anatomy Building

Terrace and Portico of Anatomy Building

There is a progressive differentiation of angioblasts, beginning in the periphery of the area vasculosa at the stage of two somites; the cells gradually appearing nearer and nearer the embryo, until, at the stage of five or six somites, angioblasts differentiate in the axial line of the embryo as forerunners of the endothelium of the heart and aorta. The heart, aorta, and main vessels of the embryo differentiate *in situ* from angioblasts, and increase by the addition of newly differentiated cells as well as by the cell-division and by the sprouting of their endothelial walls. The amount of the differentiation of new cells grows progressively less but at what stage it ceases is not known. There is thus established the fundamental morphology of the vascular system.

Blood-vessels arise by the development of a new type of cell, the vasoformative cell of Ranvier, or the angioblast of His. This cell produces the first fluid of the blood; thus, endothelium is primary and blood-plasma secondary. Since there is a tissue fluid before angioblasts arise, endothelium is from the start a membrane between two different fluids, tissue-fluid and plasma. Moreover, the process of liquefaction is intracellular, that is, it can be seen in chains of single angioblasts which become vessels and it can also be seen to take place in the sprouts which are processes of cells, hence the lumen of vessels is embryologically intracellular and thus not a tissue-space.

In the living chick of the second day, it can be seen that both angioblasts and the endothelial cells give rise to red blood-cells. Erythroblasts begin in the chick in the vessels of the outer margin of the area opaqua in the stages of from seven to eleven somites. In the area pellucida, where they can be seen in the living specimen, angioblasts differentiate during the stages of from five to eleven somites, while the vessels form and erythroblasts begin during the stage of from eleven to fourteen somites. The heart begins to beat at the stage of ten somites and the circulation starts when the chick has sixteen to seventeen somites.

During the past year, I have been continuing these studies on the living chick, and have found that it is possible to mount the entire blastoderm on a large cover-slip, one measuring 42 by 50 mm., throughout the third and fourth days of incubation. The cover-

slips must be entirely free from grease or the membrane will not flatten out on the glass. From the fifth day on, the chick is too heavy to mount in the hanging-drop form, but if the specimen be transferred to a dish of Locke-Lewis solution, the amnion can be opened, the allantois pushed aside and the yolk-sac cut off close to the embryo and then spread out and mounted. The circulation, of course, stops but the membrane can be mounted and kept alive certainly for from three to five hours. So far, I have studied these living membranes only through the first seven days of incubation. It is an advantage to mount the chick with the membranes because the preparations are all fixed after the vital studies have been made and many of them are stained and mounted *in toto*. If the embryo has been left attached, it can be cut off in the alcohol and then the entire ectoderm can be dissected off from the area vasculosa. The specimen is thus made thinner and much easier to analyze. When the embryo has been cut away at the start, the ectoderm clings too closely to the specimen to be taken off and makes one more layer of stained cells in the final specimen.

I have found it a great advantage to study the embryos with a vital dye and add 1 to 3 drops of a 1 per cent aqueous solution of neutral red to 10 cc. of the Locke-Lewis solution, making a dilution of possibly 1 to 10,000 of the dye, or less. This may be termed the physiological dilution of the dye.

After the specimens have been studied, they are fixed by floating the cover-slip, embryo down, on Bouin's picroformal, and are then kept in 70 per cent alcohol until all the picric acid is removed. They are then stained in hematoxylin and counterstained in eosin with a little orange G. This fixation is excellent for the granulocytes, but quite worthless for the erythrocytes after the primitive stage. After fixation in Bouin's solution the young erythrocytes show only a widemeshed reticulation having no relation whatever to any of the substances that can be made out in the living cell. No fixation of the blastoderms is adequate to follow the changes in the red cells, but they can be identified best after fixation in the vapor of formalin if not applied too long. I use it for from ten minutes to half an hour. In this the hemoglobin is well preserved but not the basophilic cytoplasm and indeed the earliest traces of hemoglobin which can be

seen in the living cell by a distinct yellow color cannot be detected in the fixed specimens. Helly's fluid, which preserves the basophilic substance better, cannot be used, because the blastoderms float off from the cover-slip almost immediately and wrinkle so that they can never be studied as a section with an oil immersion lens.

In connection with the study of these blastoderms, a drop of blood is drawn from the vessels when the egg is first opened and used for a film. These films of blood are studied vitally by Pappenheim's method. They are made as follows: A clean glass rod is dipped into a dye and drawn across a perfectly clean glass slide. The two dyes which I have used are neutral red and brilliant cresyl blue, made up either in a 1 per cent aqueous solution or in a saturated alcoholic solution. The even film of the stain dries quickly and its strength is estimated by the color. The film must not be dense enough to stain any nuclei. A drop of blood is then drawn out with a fine glass canula, placed on a cover-slip which is then inverted on the film of stain, ringed at once with salvoline, and placed in a warm box. The vital stains develop slowly, on an average in ten minutes, and if permanent preparations are wanted, the specimen is watched under an oil immersion lens until the staining is best, then the cover is drawn off from the slide and the film of blood counterstained with one of the blood stains. I have used Wright's eosin-methelene blue. In blood from chicks on the second and third days of incubation the amount of the specific substance of the early red cells, or megaloblasts, stainable in the vital dye is so massive that it is necessary to differentiate the specimens after staining by Wright's method. This can be done in absolute alcohol and the decolorizing stopped with xylol. The white cells are so very unevenly distributed in the vessels of the early blastoderms that no film of blood represents adequately the amount of differentiation for this stage. Hence, each stage must be studied by both methods, by a survey of the total area pellucida and by drops of blood with specific stains.

In these studies, it can be seen that there are three different strains of blood-cells: first, those that arise from endothelium, which include both the red cells and the monocyte strain of the white cells; second, the granulocytes; and third, the lymphocytes. The red cells begin to differentiate on the second day of incubation.

On the third day the endothelium gives rise to the monocytes, that is, to the large mononuclears and the transitional forms of Ehrlich. In two different specimens I have seen an occasional monocyte on the second day but the process becomes active only on the third day. The group of the monocytes of the blood is especially well illustrated by Pappenheim on his Plate 1 (2), as the third row of cells, and as the fourth and fifth rows on Ferrata's Plate 12 (3).

At the same time that the endothelium gives rise to the monocytes, namely, beginning on the third day, it gives rise to a much more numerous extravascular group of cells, identical with the monocytes, which are the clasmatocytes of the connective tissues. On the third day also the granulocytes begin to differentiate as a new type of cell from the mesoderm. These cells develop a specific type of granulation and wander into the blood-vessels. The third strain is the lymphocytes. These I have never seen differentiating in the wall of the yolk-sac, but they begin to appear in the blood-stream on the fourth day, but do not become marked until the fifth and sixth days. It may be that they arise only within the embryo itself.

ERYTHROBLASTS

In these studies it has been possible to establish a criterion for a primitive red cell. As was discovered by Pappenheim (4), the primitive red cell has a basophilic, azurophilic cytoplasm so finely granular as to appear like ground glass. Fixed to show this basophilic cytoplasm, the cell looks like a single angioblast. In the living cell a droplet of yolk is occasionally to be seen. If, however, one stains the cell supravitally with either neutral red or with brilliant cresyl blue, there appears a very massive granulation which at first completely fills the cell. This granulation is completely soluble in alcohol and in all of the usual fixatives, it disappears also in the vapor of formalin. If, however, it be stained with neutral red or with brilliant cresyl blue, it becomes insoluble in methyl alcohol and hence can be seen in films stained with Wright's eosin-methelene blue. For these double stains brilliant cresyl blue is slightly better. This special granulation is then very easy to bring out in films of blood. It is not so easy to stain in the total blastoderm, because the dilution which stains the neutral red granules of endothelium, the yolk and all of the stainable substances

of the clasmatocytes, that is, the dilution of 1 to 10,000, is too dilute to stain the granulation of the reds, but it does, nevertheless, make it just visible. The primitive red cell in the living blastoderm can be stained, however, by injecting the dye directly into the blood-stream; or if a drop of a 1 per cent solution of neutral red is put on the blastoderm for a few seconds and then washed off with clear Locke-Lewis solution, the red cells show the stain well.

The question must come up as to whether the stainable substance actually exists in the living cell in some state from which it is precipitated by the dye, just as Mott has shown that Nissl substance in its stainable form develops only as the nerve cell dies. The criterion I have used for the actual death of the cell is whether the nucleus stains or not, and this specific substance does stain in dilutions which do not stain the chromatin of the nucleus at all; the exact dilution necessary to stain it must be worked out. When Israel and Pappenheim (5) first described the vital staining of substances in erythrocytes, they thought that the staining commenced only as the cell began to die. This may be true.

For the permanent films of blood on the second and third days, the granulation is so dense that after counterstaining with Wright's stain, the cells must be differentiated in absolute alcohol, the decoloration being stopped with xylol.

On the second and third days the red cells being megaloblasts, both the granulation and the basophilic cytoplasm completely fill the cell. On the fourth day a narrow rim of clear cytoplasm appears in many of the cells, showing hemoglobin around the edge free from granules, while the granules make a very dense rosette or wreath around the nucleus. These rosettes are very characteristic and in stained preparations they greatly obscure the nucleus. By the fourth day the red cells have no longer the somewhat uniformly round shape of the earlier stage and there is no longer a comparative uniformity in size, but rather there are many much larger forms together with many small irregular or oval cells. This period of great variation in size is a stage of active division of the cells as well as of growth of individual cells. In the small oval cells, the rosettes are oval and in division the rosettes divide, so that each daughter nucleus is surrounded by a wreath of granules before the cells separate.

On the fifth day a few of the red cells begin to show a diminution of the granulation, some of the cells grow much larger and the granules and rods begin to spread out into the cytoplasm, the cells showing the polychromasia and the reticulation which is known to be characteristic of the so-called reticular forms occurring in anemias in human blood. By the seventh day there are large numbers of the cells in the reticular stage, while there are still many of the primitive cells and the wreath forms. Gradually the amount of the basophilic cytoplasm and of the vitally stainable granulation decreases while the hemoglobin increases. Finally, the basophilic cytoplasm disappears, but a small amount of the specific granulation remains in each erythrocyte. At the time of hatching and for three days afterwards, all of the red cells in the circulating blood show from one to eight or ten vitally stainable granules. I have not carried the studies further nor studied the stages between the seventh day of incubation and the time of hatching. It is clear, however, that one can work out the types of cells that are characteristic for each stage of the developing chick. Of course at any stage there are some cells characteristic of preceding stages. On the second day only the primitive stage is present and then with a given increment of time the different stages in the development of this specific granulation are added. When such a study has been made for a mammalian form and especially for the human embryo, as is now feasible, we shall be in a position to estimate just how primitive are the cells that appear in the circulation in anemias.

The first account of the staining of the specific granulation of the red cells which I have been able to find is in a paper by Israel and Pappenheim (5) in 1896, in which they say that if a few dry grains of neutral red are placed on a slide and used for a film of fresh blood, there will appear a granulation in some of the red cells just as the cell begins to die. In 1901, Bettmann (6) described the use of vital neutral red in the staining of red cells in pathological conditions, but did not discriminate between a staining of the nuclei and the specific granulation around it. Three years later, Rosin and Bibergeil (7 and 8) described the methods of vital staining and the dyes to be used, but it was not until 1907, that we have a clear account of the vitally stainable granulation of the red cells. In 1907, there appeared three

papers in the *Folia Haematologica*, one by Cesaris-Demel (9), one by Pappenheim (10), and one by Ferrata (11), in which the vitally stainable granules were described and illustrated. Cesaris-Demel showed the stage of the wreath around the nucleus, not, however, in as primitive a stage as on the fourth day of incubation in the chick. He showed also the reticular stages and the final stage of a few granules. He distinguished between the deeply staining granules and the more faintly staining filaments.

The primitive basophilic cell, which is the first red blood-cell, was first differentiated by Pappenheim (4) and called the megaloblast. It has a basophilic cytoplasm, and a large nucleus, poor in chromatin and with a conspicuous nucleolus. All the stages of the development of this cell as far as concerns the decreasing of its basophilic cytoplasm, the increasing of its content of hemoglobin, and the changes of its nucleus have been worked out with the eosin-azur technique in final perfection by Pappenheim (2), Ferrata (3), Danchakoff (12), Maximow (13), and Weidenriech (14). The development of this cell with reference to its specific granulation is now necessary to complete its life history.

In the chick, it has been shown that all of the primitive blood-cells are megaloblasts which become erythroblasts as soon as a trace of hemoglobin can be made out. These cells are derived from angioblasts and from endothelium. As far as the specific granulation is concerned, the first stage, on the second and third days of incubation, has the granulation throughout the cell; from the fourth to the sixth day, there are the rosette or wreath forms in which the granulation is around the nucleus. On the seventh day the reticular forms begin. All these stages show diffuse basophilia. It will be possible to tell with further studies just when basophilia and the reticular forms disappear in the majority of the red cells. At the time of hatching all of the cells in the circulation have acidophilic hemoglobin-bearing cytoplasm with a few vitally stainable granules. It is of course clear that at any stage in development, while the majority of the cells are in a specific phase, a few of the earlier types may be found. In normal human blood about 1 per cent or less of the erythrocytes show a few vitally stainable granules.

The question which must come up first in connection with this

granulation is its relation to the so-called basophilic punctation, and both Pappenheim (2) and Ferrata (3) agree that these two substances are entirely different. The basophilic punctation stains in azur after fixation. Ferrata thinks that it is an abnormal clumping, "conglobation," of the azurophilic cytoplasm and he shows the gradual production of the punctate forms in red cells after experimental lead poisoning on his Plate 8. It is thus easy to see why basophilic punctation does not occur in embryonic blood, while the vitally stainable granulation is on the other hand specifically characteristic of development.

Another point in which this specific granulation may prove of interest is that it offers a chance to study the development of hemoglobin in the cell by testing the granulation for the presence or the absence of iron. Both the azurophilic cytoplasm and the granulation disappear as hemoglobin develops, but the granulation alone is characteristic of the red cell as distinct from all other blood-cells.

In the developing blood there are always a few cells containing the Howell-Jolly bodies. These are fragments of nuclei staining just like chromatin, which were discovered by Howell (15) in 1890, in a study of the blood of the cat after hemorrhage. Of course the corpuscles of the chick are all nucleated, so that the question of the extrusion of nuclei does not come up, although an occasional cell, from the very beginning of the formation of blood on the second day, shows a fragmented nucleus. I interpret such cells as dead. They are to be found in the early blood islands before the cells become free and are very interesting as showing that cell death occurs in the early stages of marked cell division and growth.

ORIGIN OF MONOCYTES AND CLASMATOCYTES FROM ENDOTHELIUM

The separation of the clasmatocytes as a distinct type of cell of the connective tissues is due to Maximow (16). He showed that by introducing two sterile cover-slips under the skin in rabbits, one could separate three types of cells by the speed with which they passed between the covers, leucocytes appearing first, a special cell, the clasmatocyte, wandering in during the first nineteen hours, and the fibroblast in from two to four days. Then he showed that the clasmatocyte was specifically sensitive to neutral red (17), while

Bouffard (18), Goldmann (19 and 20), Evans (21 to 24), Schulemann (22 to 24), and a large group of workers have demonstrated that it is the cell of the connective tissues most specifically differentiated to phagocytize and store particulate matter. The specific reaction of vital neutral red to this cell is that the dye stains certain granules of the cell and certain large fluid spheres which are called vacuoles, the so-called "neutral red granules and vacuoles" of Lewis and Lewis (25). These vacuoles are organs into which the cell passes phagocytized particulate matter. In the vacuoles the fine particles which the cell has taken up become clumped and, as Evans and Scott (26) have shown, may even be recrystallized.

Aschoff and Kiyono (27) then showed that an identical reaction to a vital dye could be obtained by certain cells of the blood, namely the group Naegeli (28) has called the monocytes, which are the large mononuclear and transitional forms of the Ehrlich school. Thus they distinguished and related histiocytes of the blood and histiocytes of the connective tissues. Moreover they regarded the histiocytes of the blood as of endothelial origin.

Pappenheim (2) and Ferrata (3) have illustrated the separation of the monocytes, the leucocytes, the lymphocytes, on purely morphological grounds, believing that there is a common stem cell, a hypothetical hematoblast for them all. Aschoff and Kiyono separate the monocytes, calling them histiocytes of the white cells on a physiological basis, and I think that I can demonstrate on a fundamental embryological basis that the monocyte and clasmatocyte are identical cells, derived from endothelium and making one of the three great groups of connective tissue cells that contribute to the blood.

If a blastoderm of the third day of incubation be stained in vital neutral red, the endothelium stands out with numerous granules staining in the dye which are both around the nuclei and scattered in the thin periphery of the cytoplasm. The endothelium of the capillaries and the veins often becomes reduplicated. Endothelium is more refractive than mesoderm, and this characteristic, as well as the staining of the granules with neutral red, characterizes both of these layers of endothelium. One of the cells of the inner row can then be seen to enlarge, protrude into the lumen, and develop the vacuoles which are characteristic of clasmatocytes. The periphery

of the cell then puts out a film of cytoplasm in which there is a central process more refractile than the rest and these films are in constant motion. In fact the eye is attracted to these cells both by the stained vacuoles and by the motion of the peripheral films of cytoplasm. Such a cell then gradually becomes free. The characteristic motion of the peripheral films continues, keeping the surrounding fluid moving, though the cell itself shows very little locomotion. In the study of the origin of the red blood-cells on the second day of incubation (1) it was noted that the erythroblasts formed great clumps of cells attached to the inner surface of a complete endothelium. The monocytes, on the other hand, differentiate and drop off as single cells, leaving the original endothelial cell from which they came as the wall of the vessel.

An endothelial cell may become phagocytic while it is yet in place, for I have seen them with red cells engulfed just as Maximow (13) shows for a mammal in his Figure 4 on Plate 18. This means that an endothelial cell which is actually a part of the wall of a vessel, not one of the reduplicated forms already on the road toward becoming free, may be phagocytic. That is to say, endothelium is itself phagocytic, and has, as well, the power to give off free cells which are phagocytic. In the same figure quoted above, Maximow shows three free monocytes, very characteristic, labeled Edph. He recognized them as desquamated endothelium but did not identify them as monocytes. In fact all of the early stages of the development of blood are beautifully illustrated on the two plates of Maximow in this article.

While these few cells are becoming free in the lumen of the vessel to make the monocytes of the blood, the outer row of the reduplicated endothelium divides rapidly in irregular patches, giving the outlines of the vessels an exceedingly irregular contour, very different from the smooth contour of the earlier capillaries and from the wall of the omphalomesenteric arteries which now have a single layer of smooth muscle. The clumps of cells along the outer wall of the vessel develop the vacuoles characteristic of clasmatocytes and become free as clasmatocytes. Many hundreds of the extravascular cells are formed from the endothelium to one intravascular. The extravascular forms tend to be larger and have larger vacuoles, but I have seen one of the larger cells wander into a vessel. The original

endothelium has granules that stain in neutral red; it may also have vacuoles. The free cells all have both vacuoles and granules and a differentiation of the periphery of the cell into motile films. Studied with vital neutral red, the monocytes and the clasmatocytes are conspicuous because they are stained.

Thus, in the early chick, endothelium gives rise to two groups of cells, the megaloblasts which develop hemoglobin and become erythroblasts and a strain of cells termed histiocytes by Aschoff. The extravascular histiocytes have been termed clasmatocytes, and the intravascular, monocytes. They are identical and are specifically differentiated along the line of phagocytosis. They take up particulate matter and débris in solid form which they segregate and store in certain preformed vacuoles filled with fluid. They do not store this insoluble material permanently because it is gradually returned to the circulation and excreted by the kidney. So they represent a mechanism for taking care of foreign matter in excess of the amount that the body can excrete at the time. In the blastoderms from the third to the seventh day there is comparatively little differentiation of new angioblasts in the area pellucida. In fact, in about fifty specimens, I have found only three masses of solid angioblasts. The hollow isolated vesicles made from these solid masses are, however, more numerous, indicating that this stage lasts longer than the solid stage. In one specimen of the third day of incubation there was a long mass of solid angioblasts which started to liquefy to form a vessel, and while the center of the mass was liquefying to form a vessel, two cells wandered off from the periphery as clasmatocytes. Thus angioblasts can also give rise to clasmatocytes.

If one takes the group of monocytes as they are shown in the third row of Pappenheim's Plate 1 (2), and in the fourth and fifth rows of Ferrata's Plate 12 (3), it will be seen that the group includes all of the large mononuclear forms and the transitionals of the circulating blood. Both of these types can be seen early in the chick coming from endothelium; an endothelial derivative which is larger and less vacuolated is the mononuclear cell, a smaller and more vacuolated type, the transitional. The transitional is thus shown to be a finished type of cell like the cell of the adult form, for which the term transitional is therefore a misnomer. The large mononuclear type always has an

excentric nucleus; it is distinguished most easily in the films of blood, stained with brilliant cresyl blue and counterstained with eosin-azur. It lacks the specific granulation of the erythroblast and has a very clear distinctive blue cytoplasm in Wright's blood-stain. With the group of the clasmatocyte in the connective tissues, Maximow divided the cells into resting and active cells. With the group in the blood, it is not wholly clear whether the larger or mononuclear forms are resting or are old forms. In the embryo, the large forms appear less specifically differentiated. Both forms can be seen in the living chick to come from endothelium. Thus the clasmatocytes (histiocytes) are derivatives of endothelium, developed specifically along the line of phagocytosis and storing of particulate, solid matter and possessing a certain type of motion of the cell *in situ* and very slow locomotion.

THE GRANULOCYTES, OR LEUCOCYTES

On the third day granulocytes also begin, represented by the cells which are analogous to the neutrophilic myelocyte of mammals. In the chick the granulocyte with fine granules is pseudo-eosinophilic. The first sign of the beginning of the granulocytes is that a cell appears close to a vessel which cannot be distinguished from a single angioblast. I have not found in these cells any substance stainable in neutral red except the specific granulation which stains paler than the granule of endothelium, but am not yet entirely sure that this will be a sufficient distinguishing mark between this cell and a single angioblast. When, however, such a single cell divides there is no longer any difficulty because two angioblasts stay together while two granuloblasts separate. This criterion is not adequate when one has sections only, but in watching the living membranes or in studying them after fixation, where every cell of an entire area can be seen in its relations to other cells, it is sufficient. Such material has obvious advantages over sections. Thus, from one cell comes a clump of four or more cells with a dense azurophilic cytoplasm, the stem cell of the monophyletic school, lying near a vessel. These cells then show the following changes: The nuclei become excentric, while the center of the cell is occupied by the centrosphere made very obvious by the development of fine granules, staining pink in neutral red, always arranged in a crescent around

the centrosome. Thus, there is a nucleus on one side, a clear spot in the center of the cell, and on the other side this crescent of fine granules. The granules are entirely motionless at the start, there is none of the active streaming of the granules which is always associated with amœboid movement and which must be associated with a fluid state of the cytoplasm. The cell itself, however, does move, but very slowly, directly toward the vessel. One of the cells reaches the wall, half-way between the endothelial nuclei, and then one can see the wall bend inward, until finally the cell enters the lumen. The rest of the clump line up behind the first and also pass in. Thus, these granulocytes show a specific chemotactic reaction at once. Throughout these early stages the granules are arranged characteristically around the centrosome. Thus, the specific granulation of the red cell is arranged around the nucleus, of the granulocyte around the centrosome, while the granules of the endothelial cell are scattered throughout the cell. Even in these early stages the nuclei of these cells become indented, the concave side always being toward the centrosome, so that the primitive cell may soon be regarded as a leucocyte.

In the case of the monocytes and the clasmatocytes, both of these cells can be readily found differentiating and dropping off from the endothelium, but no relation to endothelium can be made out in the case of the granulocytes. They are near vessels but never form a part of their wall. It was shown by Dantchakoff (12) in 1908 that the granulocytes are an extravascular cell in origin.

There are no eosinophils on the third day. The eosinophilic granule of the chick's blood is in long rods. During the first seven days I have seen only a few in the circulation and have not found them differentiating in the area pellucida. Probably further study will bring them out, since they are known through the work of Dantchakoff (12) to develop in the area opaqua of the yolk-sac. The mast cells I have not seen at all in the first seven days, and Maximow (29) found that they develop late in mammals.

From these observations one may offer the theory that the two stem cells, first the angioblasts with their power to give rise both to red cells and to histiocytes in the larger sense, and second the granulocytes, are cells whose common ancestor is a mesenchyme cell instead

of a differentiated stem cell or hematoblast. In other words, the cells of the blood are not so sharply marked off from the cells of the connective tissues as to have a specific, common stem cell. At least one would have to prove that the differentiated cells which normally made the syncytial masses of angioblasts could be made to develop granulocytes. The argument for the mesenchyme cell as the stem cell for the three distinct strains of cells which contribute to the blood, is that three such groups can be isolated embryologically and they correspond to a functional classification. At least one may say that no common differentiated stem cell has been adequately demonstrated.

LYMPHOCYTES

In these studies of the development of blood in a living form, the account of the origin of the lymphocytes is very incomplete. The lymphocytes make a group of cells ranging in the mammal from the size of a red cell up to cells twice the size. Likewise in the chick the lymphocytes are the smallest cell. When the cell first appears, all of them are of the small size. The cell has a characteristic nucleus and its cytoplasm contains a few azurophilic granules, discovered by Michaelis and Wolff (30). The living cell has a nuclear membrane which is more distinct than in any other cell, but that this criterion is a difficult one to go by can be realized readily in connection with the fact that all nuclei become distinct as a cell dies. The cytoplasm of the lymphocytes contains but few granules and they do not stain readily in neutral red, but can be made to do so by increasing the amount of the dye or the time of staining. From these facts it is less readily discriminated than the other types. The reactions of lymphocytes in tissue cultures have been described by Lewis and Webster (31). In Wright's stain, the early lymphocytes are exactly as distinctive as in adult blood. The first forms are of the small variety. I have seen a few on the fourth day, more on the fifth and sixth. In the blood smears, they occur in small clumps. The chromatin of the nuclei is very dense and has a peculiar violet reaction with eosin-azur. I have never found any indication of their differentiation in the area pellucida, thus it may be that they form only within the embryo itself rather than in the yolk-sac. However, a more extensive study of the yolk-sac may bring them out. All of the evidence from

the study of this cell in the adult is that it differentiates extravascularly from reticulum. The only evidence, then, of significance in these studies in regard to this cell is that it occurs later than the other two groups and hence should not be regarded as a stem cell. Thus, from these studies, I would stress the use of the three names of white cells as specific for the three distinct groups, the leucocytes, the monocytes, and the lymphocytes.

In these studies it is very plain that each white cell, as it first appears, is differentiated; while the red cells pass through a long stage of maturation. The first erythroblasts can be told as early stages of the red cells by a specific granulation, but the cell itself passes through a long series of stages before it is the erythrocyte of the adult blood. Of the white cells, the monocytes are a phagocytic type, like the cells of the adult before they leave the wall of the vessel, the endothelium itself being phagocytic; the granulocytes develop their specific type of granulation early and soon begin to be leucocytes, and the first lymphocytes are distinctive. When, however, all of these three types of white cells begin to divide, the discrimination of all of the young cells is by no means easy, as the entire history of hematology attests. From this it can readily be seen that one must continue these studies of the development of blood in these living forms, watching especially the young cells just after division in all the stages of incubation, before one can adequately master all of the types of cells that are to be seen in bone marrow. In a drop of blood taken on the third day of incubation it is possible to tell all the cells apart, — later it becomes most difficult. It is the study of the maturation stages of each group of cells by means of the eosin-azur technique that has been the great contribution of the monophyletic school. To this study must now be added certain specific criteria that come out through the method of applying dyes to living cells; and we must now follow the stages of the cells with these vital dyes through the different embryonic periods.

The postulation of three strains of blood-cells on the basis of embryology fits in with the functional groups as we now know them. The endothelial or angioblastic group represents first the hemoglobin-bearing cells, and second that group of the blood-cells which

exhibit a special property of endothelium, namely phagocytosis. The monocytes have this power of phagocytosis, they possess a peculiar type of motion *in situ* with very slow locomotion. The granulocytes possess a high degree of amœboid motion, with speed and a flowing of the granules. They respond to chemotactic influfluences, are also phagocytic, and have functions probably related to their specific granulations. The lymphocyte strain, as Murphy (32 to 34) has shown, are separated off physiologically by their being more sensitive to X-rays and to the emanation of radium than other normal cells. Moreover, he has shown that they are related to immunity toward certain forms of tumors as well as to certain types of infection.

The study of the blood-cells is a part of the study of the cells of the connective tissues. The erythrocytes are the only type that function only within the vessels. Of the other group from endothelium, the histiocyte in the larger sense, the vast majority make the clasmatocytes of the connective tissues, which are the mononuclear forms and the actively phagocytic forms of subacute infection, the resting and active wandering cells of Maximow. A few of this group make the monocytes, that is, the large mononuclear and transitional forms of the blood. Of the granulocytes, which all differentiate extravascularly, the neutrophilic leucocytes pass into the vessels in the largest numbers. Of the eosinophiles very many remain in the tissues, while the mast cells never enter the vessels in most animal forms. By mast cell is meant a cell of the connective tissues occurring along vessels, along nerves, and between muscle fibers, having a special, metachromatic, basophilic granule. The so-called mast cell of human blood has been shown by Weidenreich (35) to be a degenerating cell without any centrosome. The lymphocytes are for the most part extravascular, arising in the lymph glands and in the follicles of the spleen and in very numerous follicles in the various organs either associated with lymphatic capillaries or not. Thus, the differentiation of three strains of blood-cells, the endothelial strain, the granulocyte strain, and the lymphocyte strain, that can be made out in the early stages of the chick embryo, can be shown to correspond with a functional grouping as far as we yet know the functions of the types of blood-cells. Moreover, the origin of the cells of the blood can be

shown to be but a part of the study of the great groups of wandering cells of the connective tissues, the only type which function only intravascularly being the erythrocytes.

The method of studying blood with vital dyes, beginning with the stages of the embryo when the cells first appear, gives a very great advantage in following the maturation of specific cells and gives a chance of analyzing the complicated young forms which it is necessary to recognize in order to understand bone marrow.

The group of the red cells is characterized by a specific granulation stainable in certain vital dyes, possibly one should say precipitated by these dyes. This substance is at first throughout the cytoplasm, then in a wreath around the nucleus, then in a reticular form, and finally in scattered granules or droplets. The arrangement of this granulation around the nucleus should be stressed, although the substance is of cytoplasmic not of nuclear origin. Red cells with nuclear fragments, Howell-Jolly bodies, can be shown to be dying cells. The strains of white cells, clasmatocytes and monocytes, that come from endothelium, are characterized by certain granules and vacuoles stainable in very dilute neutral red. They are scattered diffusely throughout the cells. The granulocytes are characterized by the arrangement of their specific granulation with reference to the centrosome. The lymphocytes are less sharply characterized morphologically, but have somewhat distinctive nuclei and granules stainable in azur.

This work is a part of the new subject of experimental cytology which seeks to analyze cells by means of specific criteria and to use these criteria to study the reactions of cells to normal and abnormal conditions.

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OSTEOMYELITIS

By

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[OUTLINE OF THE PAPER]

Three points were developed: (1) the conditions of pathologic physiology; (2) the conditions of pathologic anatomy; and (3) the treatment of osteomyelitis.

1. THE CONDITIONS OF PATHOLOGICAL PHYSIOLOGY IN BONE

The principal characteristics of infections of bone depend upon the structure of the tissue. Its vitality is low, its blood supply relatively poor, the nutritive canals are very narrow and inelastic, the ground substance is practically impermeable, and its metabolism is very slow. These facts explain the frequency of necrosis, the changes in the structure of the bone, and the difficulty of therapy in those infections which are hard to reach and whose real extent it is impossible to discover.

The infection is of local origin after traumata, operations, or infections. It is of general origin in the septicemias of staphylococcus, streptococcus, or typhoid infections. The only remarkable point is that certain infective agents very rarely localize in bone, while certain forms of staphylococcus osteomyelitis last during the whole life of the individual.

2. THE CONDITIONS OF PATHOLOGICAL ANATOMY

The macroscopic pathological anatomy is easily seen in the bony changes in infected amputation stumps. (Many lantern slides of cases of this kind in wounded soldiers were projected. They demonstrated terminal osteomyelitis and lateral osteomyelitis—extending up the shaft — for a considerable distance from the seat of infection.) These two forms must not be confused with the exostoses arising from the periosteum which have not the same form nor the same location. The former are infections, the latter are faults of the operator.

Osteomyelitis is characterized by a complete irregularity of bony growth. It is neither compact tissue nor soft tissue, but a production of spongy bony tissue in the medullary canal, under the periosteum and even outside. This osteitis is several centimeters in length and its limits are often irregular. In the lateral sort a newly formed bony cylinder extends far up under the periosteum. In certain points rarefying osteitis is complicated by necrosis of which one can follow the formation.

3. THE TREATMENT OF OSTEOMYELITIS

The treatment of osteomyelitis is preventive and curative, surgical and medical. In *traumatic* osteomyelitis the preventive measures are operative asepsis and, in amputation, making the flap sufficiently long to cover the bone completely. Several lantern slides showed, in amputations of the leg, the fibula too long and the consequent hindering of the reunion. The same thing was shown in amputation of the thigh. In such cases it is necessary from the beginning to use traction on the soft parts.

The *cure of spontaneous acute osteomyelitis* in young persons is difficult. Surgical treatment by immediate and extensive resection leads to relapses. Attempts at autovaccination or stock vaccination with staphylococcus and also attempts at "proteinic shock" have given very inconstant results, and favorable results, while more frequent, are not constant. Some cases have even been cured without surgical intervention, but their future course is not yet known.

In *chronic* osteomyelitis, disinfection of the wound with Dakin's solution is long and difficult, and exposed to frequent check, for the subjacent infection of the bone cannot be reached, and the organisms spread to variable distances in the wound. Curettages and the resection of the diaphysis as far up as the medullary canal makes reinfection liable. The transformation of the suppurating cavity to a large flat surface is the best method. If it is aseptic, a graft of living muscle with healing by primary intention is often efficacious.

In cases of osteomyelitis in amputation stumps one ought to remove only a minimum of the infected tissue and not touch the distant lateral osteitis which heals by itself.

In spite of all these methods, osteomyelitis remains the most

terrible, the most tenacious, and the most rebellious of surgical affections of the bone. One must reckon its duration by years, and it can never definitely be said that a patient has recovered.

SUPPLEMENTARY REMARKS

The factor that makes it difficult to judge the value of vaccination in spontaneous osteomyelitis is that the evolution of the disease varies greatly in different cases, and that there is not always anything in the first symptoms that would make it possible to predict the later course of development. Thus certain spontaneous osteomyelitis cases grow worse abruptly, with fatal consequences. On the other hand, local symptoms apparently serious, may disappear spontaneously. So when one surgeon reports a case of cure by the use of vaccine, another immediately protests, saying that he has seen similar cases cured without either vaccination or operation.

It would seem, however, that in certain varieties of these infections very great improvement, if not definite cure, has resulted from the use of vaccine.

It is very difficult to say how long this vaccination affords protection, and whether symptoms will not recur, but it may be stated as certainty that X-rays taken later would lead to a diagnosis of osteomyelitis. It rarely, if ever, happens that an acute osteomyelitis does not leave behind it disturbances in the bony structure, a sequel which the X-ray would always reveal. The question is whether vaccination performed at the very start of the disease does not check the process of the bone lesions shown by the X-ray. The problem is a complex one, but, in my opinion, it is moving toward a solution favorable to vaccination.

THE PRESENT STATUS AND FUTURE PROBLEMS OF CHEMOTHERAPY

By

SAHACHIRO HATA, M.D.

INTRODUCTION

Ever since Ehrlich with Hata published the therapeutic action of salvarsan upon spirochetosis as one of the results of his long continued study on chemotherapy, the eyes of all the workers in medicine interested in the treatment of infectious diseases have been turned to his new school. Investigation of various chemical preparations has been both experimentally and clinically applied in the treatment of various diseases in all quarters of the globe. Scientists were, at that time, working with so much eagerness and hope that Ehrlich expressed his heartfelt wishes before the XVIIth International Congress of Medicine in London in 1913, in the following words: "I might, without being set down as an optimist, put forward the view that in the next five years we shall have advances of the highest importance to record in this field of research." Ehrlich's hope was shared by many who expected that before long important progress in chemotherapy would be made. Alas for the newly introduced branch of medical science! In one year or so, the whole world became involved in one of the most devastating wars ever known. The consequence was that scientific researches and investigations were abandoned and before the war was over, Ehrlich had passed into eternity. Our former hope remains as a hope, now that more than five years have elapsed since the death of the leader of chemotherapy. But the endeavor of numerous workers in chemotherapy, exerted during the ten years since the discovery of salvarsan, has not been entirely unrewarded, for there has been a perceptible advance in fundamental research as well as in clinical application.

The first requisite that should be borne in mind in the experimental work on chemotherapy is that we must know the nature of the pathogenic viri and such viri must successfully cause experi-

mental infection in the animal body. Had there not been the brilliant works of Lister, Pasteur, Koch, and many others, Ehrlich's results would never have been obtained. Consider, then, the discovery of the virus and successful experimental animal infection of Weil's disease by Inada and his co-workers, the results of the studies on yellow fever by Noguchi of The Rockefeller Institute, the remarkable achievements of Flexner in the study of poliomyelitis, the successful animal inoculation of typhus fever and tsutsugamushi disease, which has been attained by various workers. They not only contribute to the etiological knowledge of infectious diseases, but also to further advances in the immunotherapy or chemotherapy by which these diseases may either be cured or the sources of their infection eradicated, even though no satisfactory remedies for them are yet known.

Improvements in the preparation of salvarsan have already been attempted and successfully made by Ehrlich, who discovered new preparations in the form of neo-salvarsan and the sodium salt of salvarsan. These two modifications have an advantage over salvarsan in the facility of their practical application. They have not been, however, improved in their therapeutic indices, which are most important in the therapeutic efficacy of any chemotherapeutic preparation. Ehrlich has also made studies on the metallic compounds of salvarsan. It was a few years ago that his successor, Kolle, published the fact that, of all the metallic compounds, silver salvarsan is the most efficacious. He reports that it has an even better therapeutic index than salvarsan, but the results of my tests unfortunately proved that it fell short of expectations. I have also tested the silver salts of Japanese-made salvarsan, "arsaminol." I have found that it produced no better therapeutic indices than the original arsaminol. Quite independently of Kolle's work, I have been making comparative studies with more than ninety preparations of the gold, silver, mercury, and other metallic salts combined with arsaminol, but have not obtained any satisfactory results. Among these, by the way, the silver antimonium compound of arsaminol has by far the greatest efficacy and sometimes it has proved to have better therapeutic indices than arsaminol. It still remains unproved whether or not Kolle's silver salvarsan has any practical advantage

over salvarsan with regard to its therapeutic efficacy. I have also tried the best preparations of the silver antimonium salts of arsaminol on many cases, but I have not found that they possess any remarkable advantages over arsaminol.

There is, however, one advantage that such metallic compounds of salvarsan have: that is, they are more stable than salvarsan, or in other words, they are less liable to turn into poisonous substances by oxidation or decomposition. Again, Kolle has prepared another derivative of salvarsan, which is known by the name of "sulphoxylate." This is said not to undergo any changes even when it is made into a solution. I have had as yet no experience with this. Giemsa has also prepared a derivative of salvarsan, "arsalyt" or "bismethylamino-tetramino-arsenobenzene," which is said to be efficacious in all forms of spirochetosis, with a very high therapeutic index. But I have as yet heard nothing further about the results of its practical application. These facts indicate further possible improvement for the preparations of salvarsan derivatives which have higher therapeutic indices and greater facility for practical purposes.

DISEASES AMENABLE TO SALVARSAN TREATMENT

When viewed from the clinical standpoint, there has been great progress in the range of application of salvarsan within the last few years. Salvarsan is nowadays employed with more or less efficacy for the treatment of the following diseases: spirochetosis, trypanosomiasis, malaria, amœbic dysentery, leishmaniosis, bacterial diseases, diseases caused by unknown viri.

1. Spirochetosis. We can here enumerate relapsing fever, frambœsia or yaws, Vincent's angina, avian spirochetosis, and rat-bite fever. These are, as a rule, cured by one injection of salvarsan. In these cases, salvarsan attains indeed its ultimate end of *therapia sterilisans magna.* Rat-bite fever is found chiefly in Japan, and it may also be found in China. The remarkable therapeutic value of salvarsan against this disease, together with the discovery of *Spirochæta icterohæmorrhagiæ*, led Futaki and Ishiwara to the discovery of the causative agent of the disease and also to successful experimental infection in animals. This is a curious example of the reversed order of investigation in the annals of medical science.

To hope for the same amazing curative efficacy of salvarsan in all the other forms of spirochetosis would be, it seems to me, too hasty. Syphilis is not so easily amenable to salvarsan at a certain stage and form of that illness. This seems to depend chiefly on differences of the biological nature of spirochetes and especially on the shelter, in which they may lie unhurt by the injected remedy. The local treatment, which Flexner lays stress on, bears a high relative importance. The intralumbar application of salvarsanized serum in syphilis of the central nervous system, which has been introduced by Swift and Ellis of The Rockefeller Institute for Medical Research, fulfills Flexner's requirement. From the results of the practical application of their method, gleaned from years of clinical experience, I have come to the conclusion that it often has far more remarkable efficacy in the treatment of the central nervous system involvements than has the intravenous administration of salvarsan alone.

I deem it proper here to say a few words on some of the newly introduced mercury preparations. As you all know, asurol is one of the very convenient mercury preparations for practical purposes, for it may be comparatively harmlessly applied to human cases in large quantity and thus a larger quantity of mercury may be introduced into the human body than when it is given in any other form. More recently another derivative of asurol by the name of "novasurol," which is a double compound of the sodium salt of oxymercurichlorphenylacetic acid and diethyl malonyl urea, has been widely employed. There are still other forms of mercurial compounds. They are mercedan (HgNa-paranucleic acid), contraluesin (a compound of gold with mercury), cystinmercury, etc., which are used for experimental purposes. There is reason to hope that there will be improvement in mercurial compounds.

Now to return: Arsenics have been contraindicated in putrid bronchitis, bronchiectasis, and gangrenous pneumonia, but recently salvarsan has been known to produce remarkable improvement in these pulmonary affections. Such improvement may be due to the spirocheticidal action of salvarsan, which acts against the saprophytic spirochetes that may be found in the putrid foci in the lungs. Here these saprophytic spirochetes may also play a certain part in

the acceleration of putrefaction. Since these pulmonary affections have been found amenable to salvarsan, there have been many reports regarding spirochetes in the respiratory system.

Another form of spirochetosis, ulcus tropicum, which is known in South China by the name of Annam ulceration or Cochin sore, has been reported by many observers to have been successfully cured by salvarsan or its substitutes.

It is very interesting to notice that the leptospira group, which biologically are closely allied to spirochetes, have a remarkable resistance against saponin, which is a strong spirochetolytic agent, and that their infection cannot be cured by salvarsan, the specific remedy for all other spirochetoses. I have tried various chemical preparations in the infection from *Leptospira icterohæmorrhagiæ*, but none of them have been found efficacious.

2. *Trypanosomiasis.* It is a well known fact that salvarsan and its derivatives have some efficacy against all kinds of trypanosomiasis. Nowadays, arsenophenylglycin is no longer employed in sleeping sickness, but salvarsan or its substitutes are in vogue. In the last stages of the disease when there is involvement of the central nervous system, local treatment is needed. Haendel Joetten of Gesundheitsamt reported that a proprietary remedy, Bayer 205, prepared and offered for sale in Germany in 1920, was a strong trypanocidal agent. Mayer and Zeiss of the Hamburg Institute for Tropical Medicine verified the efficacy of this remedy by their experiments. This preparation is said to be efficacious against all kinds of trypanosomes, except *Trypanosoma lewisi* and *Schizotrypanosoma cruzi*. The results of its application to various kinds of experimental animals showed that the therapeutic indices vary between 1:20 and 1:40. Mayer even obtained the favorable figure 1:160 in *Trypanosoma gambiense*. Although this species of *Trypanosoma* in the infected mouse is relatively easily curable, the therapeutic indices of either salvarsan or silver antimonium arsaminol varied between 1:30 and 1:33, and they never reached the figures shown by Bayer 205. I myself have had no experience with Bayer 205, nor have I heard anything of its practical application. Should the above-mentioned results be obtained in the human cases or in trypanosomiasis of large animals, it would be indeed a remarkable achievement.

3. Malaria. Although salvarsan is efficacious in all forms of malaria, yet the sterilization involves only the schizonts, and not the gametocytes. Therefore, salvarsan cannot be said to be superior to quinine. Salvarsan may, however, be employed in quinine-fast cases and also in a combination treatment with quinine, so that a more powerful effect may be obtained.

4. Amœbic Dysentery. This is a disease widely distributed over the entire area of China. Salvarsan has been found sometimes to produce a very remarkable improvement in this form of disease, but in some cases it has been found entirely powerless. Whether or not this uncertainty of the efficacy is due to the differences in the developmental stages or of the strains of amœbæ, is still to be learned. At any rate, salvarsan has given place to emetin in the treatment of amœbic dysentery. Emetin was first used by Rogers. Of all the alkaloids that are found in the ipecacuanha root, this one is the most efficacious, but investigators are still searching for a satisfactory form in which to employ it. In order to avoid the by-effects of emetin, emetin bismuth iodide has been prepared, which is considered to pass the stomach unchanged and be digested by the intestinal juice before its action is developed. Emetin acts not only on amœbæ but, to a certain extent, on *Paragonimus westermannii*, or lung-fluke, and also on bilharziosis. There is much to be learned about this alkaloid.

5. Leishmaniosis. The only kind of leishmaniosis that can be ameliorated more or less by salvarsan is Oriental sore. Although there is a report that deals with the successful treatment at the initial stage of espundia, it is not yet an established fact.

There is no doubt about the efficacy of antimonium against all forms of leishmaniosis. It was formerly administered in the form of tartar emetic, either internally or locally. Better success has been attained, however, by the intravenous injection of tartar. If arsenics have any ameliorating action against leishmaniosis, they are better given in combination with antimonium. The only difficulty met with in experimental study, is that leishmaniosis cannot be developed in animals, while on the other hand only with difficulty can antimonium be directly combined with the benzene nucleus. For the time being, there is only one way of investigation open to

us. That is practically to apply a compound of antimonium and salvarsan to human cases. I have been informed of the fact that French-made "luargol" has been effectively employed on human cases of espundia in Brazil. The drug is a compound of silver, antimonium, and arsenic. If a chemical production having a stronger action than luargol should be discovered, more successful treatment of such forms of leishmaniosis as Oriental sore, kala azar, espundia, etc., may be expected.

Bilharziosis, filariasis, and similar affections which have been considered to be ameliorated to a certain extent by arsenics and antimonium preparations, may be even better treated by the above mentioned compound. It has been well known that antimonium has certain ameliorating efficacy against trypanosomiasis and spirochetosis, and, therefore, it is earnestly hoped that advance will be made in the chemistry of antimonium.

6. Bacterial Diseases. Of all the bacterial diseases, human anthrax is the only one known to have been cured by salvarsan. It was applied for the first time without any scientific basis. Its specific bactericidal property, however, was established afterwards by trying the sterilization test both *in vitro* and *in vivo*. It has been reported that salvarsan is also efficacious against horse glanders and swine erysipelas. Last year, Kolle obtained 1:4 to 1:5 therapeutic indices with a preparation obtained by combining sulphoxylate and carbamide against swine erysipelas. It is, however, still to be learned whether or not such arsenic compounds have any practical therapeutic efficacy. The sterilization of bacteria and the chemotherapy of bacterial diseases with other chemical preparations than arsenics will be dealt with in a subsequent paragraph.

7. Diseases Caused by Unknown Viri. Disease of the breast in horses is cured by one injection of salvarsan. Salvarsan has also a certain degree of efficacy in scarlet fever and smallpox of man. But it seems not to be due to the antiparasitic action of the drug, which is the first requisite in chemotherapy. Nearly all of the human diseases that are caused by either unknown or invisible viri have not been perfectly reproduced in experimental animals, and therefore, a rapid progress in their chemotherapy cannot be expected.

Hitherto I have been dealing chiefly with salvarsan or its substi-

tutes, the kinds of diseases that are amenable to their administration, and some two or three other chemical compounds have been comparatively considered. I have also dealt with certain diseases which seem to have closely related chemoceptors. I will now consider the internal and local disinfection of bacterial infections.

INTERNAL AND LOCAL DISINFECTION OF BACTERIAL INFECTIONS

Specific remedies against certain diseases that have become known empirically, such as quinine against malaria, mercury against syphilis, and ipecacuanha against dysentery, all belong to the treatment of diseases of protozoal origin. Chemotherapy as founded by Ehrlich also deals chiefly with the treatment of trypanosomiasis and spirochetosis, while the attempt to attain the internal disinfection of bacterial agents by the use of some chemical preparations such as have been tried by Koch, Behring, and others, has turned out to be futile. These facts almost caused us to conclude that internal disinfection was impossible. But this impossibility has been surmounted by the discovery of Morgenroth that quinine effects internal disinfection in pneumococcal infection. Almost simultaneously with his discovery, there were reports both by the Japanese and German observers that salvarsan has curative efficacy against anthrax in man. Study on the chemotherapy of the diseases of a bacterial nature has thus been reviewed, and further study opened the way to the discovery of chemical preparations having a bactericidal property, for use in local disinfection.

The artificial cultivation of a large number of protozoa is hardly ever attainable. The only way, therefore, to test the germicidal action of a new chemical substance against them *in vitro* is to apply it to living specimens and see the change in their motions under the microscope. By this method we may be able to see the effect of the chemical substance on the bodily constituents that might have a certain relation to motion, but its action against the chromatic substance that plays an important rôle in the proliferation may be known only *in vivo*. There are not a few cases in which a curious phenomenon is encountered, namely, that, although *in vitro* a given substance is powerless against certain germs, *in vivo* it exercises a remarkable parasiticidal action. Thus in the study of chemotherapy

of protozoa, the value of the simple and cheap method of test *in vitro* is greatly limited. Bacteria, on the other hand, can be tested for the action of any chemical substances that may be supposed to have germicidal power by cultivating the bacteria after contact with the substances in question. Thus the *in vitro* test will hold a high place in the chemotherapeutic study of such bacteria. The principle of chemotherapy is the research on the chemoceptor of the parasite. With bacteria, the direct proof of the presence of the chemoceptor can be shown by the cultivation of drug-fast bacteria, and can be made *in vitro* without employing experimental animals.

One of the most important points that should be known in the *in vitro* investigation of chemotherapy is the choice of media in which the chemical preparations will act. Common disinfectants such as sublimate and carbolic acid exercise their highest efficacy in saline, but in the presence of serum or other colloidal substances, their disinfectant property becomes remarkably weak. Those drugs that are efficacious in internal disinfection, act as effectively in serum as in saline. Secondly, there is another factor which is as necessary as the former, that is, the specific disinfecting power against certain species of pathogenic micro-organisms. Common disinfectant develops its disinfecting power universally over all the species of bacteria, but disinfectants that can be employed internally should possess an especially strong disinfecting power against a certain species of bacteria. Quinine has a very remarkable disinfecting power against pneumococcus both *in vivo* and *in vitro*, as salvarsan has against *Bacillus anthracis*.

Some years ago, Ehrlich studied the specific disinfectants against bacteria in co-operation with Bechhold and by coupling phenol or cresol with a certain halogen, they obtained disinfectants having a remarkably strong power against certain species of bacteria, for example, tetrabromorthocresol, which has a specifically strong bactericidal power against *Bacillus diphtheriæ*. They called this kind of drug a half-specific disinfectant. Later Bechhold coupled a halogen with naphthol and found that monochlornaphthol has a remarkably strong specific disinfecting power against *Bacillus tuberculosis* and tribromnaphthol against streptococci and *Bacillus diphtheriae*. Jacobs of The Rockefeller Institute substituted urotro-

pin or hexamethylenetetramine with benzyl or halogenacetyl derivatives and obtained a number of new compounds. He studied the relation between the constitution and the disinfecting power of these compounds against *Bacillus typhosus*, meningococcus, and gonococcus. As the results of his studies, he found that a number of his new preparations possessed an unusual bactericidal action, which was to be observed even in the presence of serum or colloidal substances. From his work it can also be seen, that the partial specific bactericidal action of the preparations has a certain relation to their constitution. Such fundamental biological work is most useful for the furtherance of chemotherapy, though it may not be directly applicable in practice. His work seems to have been suggested by Flexner's discovery that urotropin has a curative efficacy against poliomyelitis. In America, urotropin has been employed in the treatment of typhoid fever and Weil's disease for the purpose of internal disinfection. Here it should be noted, however, that Trendelenburg has found that urotropin develops disinfecting action by decomposing into formalin only in an acid medium.

By reviewing all the chemotherapeutic work hitherto published, it would seem very probable that internal disinfection has been obtained only in those species of bacteria that have a tendency to develop septicemia, while, on the other hand, those that cause local infection are better treated by local disinfection with the specific disinfectant. The following drugs have been found more or less effective in the chemotherapy of bacterial infections: quinine and its derivatives, acridine dyes, triphenylmethane dyes.

DRUGS EFFECTIVE IN THE CHEMOTHERAPY OF BACTERIAL INFECTIONS

1. Quinine and Its Derivatives. This is the drug first to be mentioned in the chemotherapy of bacterial diseases. It is now an almost established fact that hydroquinine and the hydrochloride of ethylhydrocuprein or optochin, is, as discovered by Morgenroth, a specific remedy for pneumococcal infection. Since this discovery, he has been studying further with quinine and found that iso-octylhydrocuprein, or vuzin, and isoamylhydrocuprein, or eukupin, have both a remarkable disinfecting action. Of these three, optochin has far less carbon content and is best adapted for internal disinfection,

especially for pneumococcus. Eukupin, which has a higher carbon content, may also be employed for internal disinfection, but it is slightly better adapted for use as a deep reaching focal disinfectant. Vuzin, which has the highest carbon content, is best fitted for focal disinfection. The latter two seem to be more efficacious against streptococci and staphylococci than against pneumococci. The specific relation of the three above-mentioned quinine derivatives against cocci is not notable. The facts that are interesting to the investigators are that there seems to be a certain relation between the sizes of the molecules and the processes of the disinfection.

There are not a few reports dealing with the successful treatment of influenza with these quinine derivatives. It seems highly probable that they should have acted against the mixed infection from pneumococcus and streptococcus.

2. *Acridine Dyes.* The action of this group of dyes against trypanosomes has been studied minutely by Ehrlich. Among the rest, diamino-methyl-acridine-chloride has the most powerful trypanocidal action, from which fact it has been given the name of trypaflavine. English investigators call it simply by the name of acriflavine. Lately, Neufeld of the Koch Institute tested the disinfecting power of this dye and found that it had a strong sterilizing power against pneumococcus and chicken cholera bacillus. Moreover, he found that diamino-acridine, which is known by the name of proflavine in English, and which has no methyl group in its molecule, is more powerful than acriflavine, which is provided with a methyl group. These two drugs have been found to develop a higher disinfecting action in the presence of serum than in saline. The fact that acriflavine has a higher disinfection in serum is indeed a paradoxical phenomenon, which can be easily proved. This fact led Langer to carry on further with the studies of this drug and to prepare new chemical substances having more methyl groups than flavine. Of these, the chloride of 2-7-dimethyl-3-dimethylamino-6-amino-10-methyl-acridine, or shortly called flavicide, has the strongest bactericidal power and its immediate bactericidal power against staphylococci is ten times as large as that of acriflavine, and against the diphtheria bacillus five times. The inhibitory power against the growth of staphylococcus that is exercised by flavicide is five times

that of acriflavine, and against diphtheria bacillus it is only twice as great. Flavicide does not increase its bactericidal power in serum as does acriflavine. Langer tries to explain the differences of these experimental results by the differences of the physical natures of the remedies as shown in solution. The difference is, in brief, that the substances having more of the methyl group have a weaker dispersiveness and therefore more immediate bactericidal power. On the other hand, those that are provided with less of the methyl group have a stronger dispersiveness and have therefore a weaker bactericidal power. In serum, however, the dispersion is remarkably interrupted and the results are that a stronger bactericidal action develops. On this hypothesis Langer concludes that acriflavine is better fitted for internal disinfection, while flavicide answers better for local disinfection. He also tries to explain the above-mentioned relation between optochin and vuzin.

The results of the further experimental investigation made by Neufeld show that acriflavine has a high internal disinfecting power against meningococci, pneumococci, streptococci, *Bacillus anthracis*, and *Micrococcus melitensis*. Acriflavine has since been used, as optochin is used, with some success in all forms of septicemia, and flavicide has been employed as a local disinfectant in eczema, furunculosis, abscesses, conjunctivitis, otitis, and wounds, and in the treatment of diphtheria carriers.

The genuine local disinfectants, such as chlorine in the series from Dakin's solution to dichloramine-T in the treatment of wounds, and choleval in gonorrhea, and yatren in diphtheria carriers, stand outside of the scope of chemotherapy, and I will mention only the disinfection of the typhoid bacillus in the gall bladder of typhoid carriers.

3. Triphenylmethane Dyes. In the chemotherapeutic treatment of the experimental cholecystitis in the rabbit these dyes have been carefully studied. But unfortunately there has as yet been discovered no drug that can be applied with success to the cases of human typhoid carriers. It was only last year that Uhlenhuth and his coworkers found by experiments with a large number of chemical substances that methyl violet and fuchsin have given the most favorable results. These drugs, however, cause a comparatively severe

inflammatory reaction in the injected tissues, and therefore, it still remains problematical whether or not they may be given to human cases in sufficiently large doses without any ill-effects.

CHEMOTHERAPY OF TUBERCULOSIS

The chemotherapy of tuberculosis has been attempted by many investigators, but there has been as yet no satisfactory result. Since the iodide of methylene blue has been reported by Finkler and von Linden, a number of drugs for tuberculosis have been reported from time to time. Above all, metallic compounds have been most frequently the object of investigation, the compounds of copper and gold being considered most promising. Some of these are cyanocuprol of Koga, gold potassium cyanide, and cantharidine-ethylenediamine (aurocantan) of Bruck. Recently in Germany the sodium salt of *p*-amino-*o*-aurophenol carbonic acid, which is a preparation in which the irritative cantharidine has been excluded from the composition, has been reported to have a certain efficacy against tuberculosis. It is largely employed in practice by the name of "krysolgan." In France, cerium salts are being widely studied. All these chemical substances have developed a remarkable curative efficacy in surgical cases of tuberculosis, such as joint or bone, but in the internal infection, such as in the lungs and in the intestines, no one of them produces any satisfactory results. Metallic compounds and metallic colloids are also employed in the various forms of bacterial infection, such as pneumonia, influenza, and septicemia. In certain cases they have been proved to be very effective, but when we come to consider the mechanism of their action, we are not certain whether they are really antiparasitic in the sense of chemotherapy, or whether their efficacy is merely the result of catalytic action.

CHEMOTHERAPY OF LEPROSY

It has long been known in India that chaulmoogra oil has a certain improving power against the symptoms of leprosy. In Hawaii, Goto employed it more than a score of years ago. Formerly it was administered only *per os*, but lately it has been employed by hypodermic injection. Much has been learned about the nature of the acid of this oil, and the greater efficacy of the sodium salt of its fatty acid

has been reported by Muir and Rogers in India, Hollmann in Hawaii, and by the Philippine Health Service. Very recently Dean in Hawaii prepared an ethyl ester of this fatty acid, which has been employed in the practical treatment of human cases first by Hollmann and second by McDonald. In 1920 it was reported that seventy-eight patients had been paroled as they were no longer a menace to public health and not one of them is thus far known to have had any sign of recurrence. The Kalihi Hospital is now known among the laymen by the name of Mount Happy. Rogers also reports that a comparatively good result has been obtained by the use of this ethyl ester. If these wonderful results should be proved by further observations, it would be an important step forward, even if the cure is wrought in only a limited number of cases.

CHEMOTHERAPY OF MALIGNANT TUMORS

Finally, I will deal very briefly with the chemotherapy of malignant tumors. All the diseases that are caused by infectious pathogenic micro-organisms are the results of infection by foreign cells other than the cellular elements of the host, and naturally they may have all their own specific chemoceptors, which are different from those of the body cells. The tumor cells, on the other hand, consist of changed autogenous cells, or in other words, they are the hostile brothers of the body cells. The chemoceptors that they have, therefore, are common to all, and it must naturally be very difficult to find the small differences in the chemoceptors of these two brother cells. But the brilliant work on eosin-selenium attained by Wassermann and the so-called tumoraffin substances (which are obtained by the combination of various kinds of metals by Neuberg and the use of choline as a chemical imitation of the action of Roentgen rays originated by Werner and Scesci) afford us a promising view of the future of the chemotherapy of malignant tumors. These have so far been studied only on experimental animals, and the trial of them in human cases is a matter of the distant future. In this difficult realm of investigation there has been as yet nothing practical, but this is also one of the interesting fields open to the exploration of the followers of chemotherapy. We have reason to hope for success.

Thus far I have, from the standpoint of the laboratory investigator, dealt with almost all the work that has been approached in the advance of chemotherapy during the last ten years, together with the problems that are now laid before the investigators. The furtherance of chemotherapy cannot, however, be attained without the co-operation of the chemist and the biologist, with untiring perseverance and financial support. The chemical substances that should prove efficacious, must then be handed to the clinicians. The attainment of final clinical success can be reached only by the hand of the clinicians, who must study the effect of the remedies with an all-pervading observation in a wide range of experience and with the closest attention. The course of disease and the nature of the causative agents are complicated and perplexing; and the final goal may in some cases not be completely realized by "therapia sterilisans magna." In that case we must be satisfied with "therapia sterilisans fractionata," or even with the "combination treatment." Again, sometimes it may be necessary to apply local treatment according to the situation of the foci. All these problems, the choice of methods of treatment, the size of dose or the avoidance of ill-effects from the drug, may require even more hard labor on the part of the clinicians than the originators of the drug used in its preparation.

In his great consideration and of his own accord, Mr. Rockefeller has appropriated an enormous sum to enable the Rockefeller Foundation to perform works of humanity. As one of its activities, this splendid institution, the Peking Union Medical College, has been established, comprising a large hospital and splendid laboratories with the latest equipment for the care of patients and for carrying on medical research. Here able medical scientists will be educated and here numerous brilliant achievements in medicine will be accomplished. On the occasion of the dedication of this College and Hospital, the Kitasato Institute for Infectious Diseases, which has a purpose similar to that of your institution, expresses the hope of fraternal co-operation for the progress of medicine. In the name of science, I thank Mr. Rockefeller, and present my cordial respects to all members of the staff of the Foundation.

CLINICAL SECTIONS

DEPARTMENT OF GENERAL MEDICINE

SYPHILIS

By

H. Jocelyn Smyly, M. D.

DIAGNOSIS

In dealing with syphilis, an early diagnosis is absolutely essential. The earlier the diagnosis, the better is the chance for cure. In primary cases, a darkfield examination for the spirochetes should be made and treatment instituted at once if this is found to be positive. In the examination of cases of syphilis, secondary eruptions should be looked for and ruled out from other skin conditions. The enlargement of lymph glands, particularly the epitrochlears, is an important finding. Further general examination should also include the teeth and size of the aortic dullness.

TREATMENT

Pyorrhea alveolaris and gingivitis should be taken care of. Frequent brushing of the teeth is to be urged, especially when patients are receiving some form of mercury. A tooth powder containing potassium chlorate is very effective. Cases with dilated aorta should receive a preliminary course of mercury and potassium iodide before the intravenous injection of salvarsan, and this is then employed with great caution.

The use of mercury, potassium iodide, and the arsenical preparations may be discussed here. The intramuscular injection of mercury, given in the form of mercury salicylate, is the most satisfactory method to employ. Potassium iodide is valuable in tertiary cases, as it hastens the absorption of scar and granulomatous tissues. In all cases of syphilis, the use of salvarsan should be urged. The dosage employed is usually 0.5 gram, given every seven days for a period of five or six weeks, mercury being given concurrently or subsequently. During the past year there were two cases of severe salvarsan dermatitis in the clinic in Peking, and so the dosage has been reduced to 0.3 gram, given in weekly injections for ten weeks.

DURATION OF TREATMENT

This is a very debatable matter, and one which is being constantly changed in the various clinics. The tendency, however, is always in the direction of extension of the period. For security it is possible that a minimum of a year's treatment for primary cases should be given. Our practice has been to give treatment in ten-week courses until the Wassermann reaction has become negative and all symptoms have disappeared, and then to advise the patient to report for re-examination every two or three months for two years. A negative Wassermann after treatment does not indicate a cure in tertiary cases, since we see it in cases with active symptoms, especially in cases of involvement of the nervous system.

A case was shown of primary reinfection as evidence of ineffectiveness in the cure of syphilis. This case was treated here in 1916 for secondary syphilis.

SYMPOSIUM ON KALA AZAR

PARTICIPANTS:

DR. OSWALD H. ROBERTSON
DR. RICHARD H. P. SIA
DR. CHARLES W. YOUNG
DR. JOHN H. KORNS

DR. ROBERTSON showed an early case of kala azar and pointed out that the clinical picture presented by this patient might easily be mistaken for chronic malaria. The different types of kala azar encountered were then briefly discussed. Special reference was made to certain cases in which marked enlargement of the spleen and liver may be present without anemia or febrile reaction. Two other cases, with cancrum oris (healing), were also shown.

DR. SIA read a paper on a simple diagnostic test for kala azar, and demonstrated its technique. The method employed consisted of adding 20 cmm. blood from skin puncture to 0.6 cc. of distilled water in a small test-tube. The mixture was thoroughly shaken and the reading made at the end of five or ten minutes. A positive test was shown by the turbidity of the mixture and the formation of a white flocculent precipitate on standing. This test has been performed by Dr. Sia on eighty-six patients suffering from various diseases, including ten cases of anemia with hemoglobin ranging from 30 to 60 per cent. It was found that positive tests were obtained only in kala azar patients and that all the cases of kala azar (sixteen in number) gave a positive reaction. The cause of the turbidity was further shown not to be due to incomplete hemolysis of the red blood corpuscles, as was believed by Ray, but to an abnormally high amount of globulin in the blood serum of kala azar patients. The term "globulin precipitation test for kala azar" was suggested by Dr. Sia to replace the so-called "hemolytic test" employed by Ray.

DR. ROBERTSON discussed the anemia occurring in kala azar and pointed out that little has been done to determine the nature of the anemia, whether it is due to increased blood destruction or whether a depression of the bone marrow function is at fault. Results of the work being undertaken on this subject by Dr. Sia (as yet incomplete) would indicate that the anemia is due to bone marrow depression.

An investigation of the cause of the bleeding in those patients with hemorrhagic manifestations revealed the fact that while the coagulation time of the blood was essentially normal, there was a marked delay in the bleeding time which was associated with a diminished number of blood platelets. This observation has an important bearing on the performing of spleen puncture. In order to make this a safe procedure we believe that the bleeding time should be tested beforehand in all cases. If a marked delay in bleeding time is found, the patient should be transfused. This brings about a shortening of the bleeding time; and spleen puncture can be safely performed.

The technique of testing bleeding time according to the method of Duke was demonstrated by Dr. Sia. Normal bleeding time with this method varies from 1 to 3 minutes.

Dr. Young reported on cultures of kala azar which he was making. He used Nicolle, Novy, McNeal medium with the addition of 0.2 per cent potassium hydrogen phosphate (K_2HPO_4) and adjusted to definite hydrogen ion concentrations. The results from several series of cultures indicated that the optimum hydrogen ion concentration for the initiation of growth of kala azar from the Leishman-Donovan bodies lies between pH 7.4 and 8.0. In obtaining cultures he used spleen puncture with a 20 cc. syringe containing 10 cc. of Locke's solution. By using media buffered with phosphate, Dr. Young thought he had obtained later flagellate and "postflagellate" forms, resembling Leishman-Donovan bodies. They seemed to be somewhat similar to the corresponding forms reported by Patton (1) for *Herpetomonas muscæ domesticæ* from the gut of flies. Such forms have not been reported previously *in vitro*. Cultures have been made, using washed but uninactivated red blood-cells of the horse, sheep, rabbit, and man in the medium. Only those containing rabbit cells grew. None of the tubes to which the sera of these four animals were added, showed growth. Inactivated cells and sera had not yet been tested. Dr. Young called attention to the success of Patton (2) and Knowles (3) in finding Leishman-Donovan bodies in the peripheral blood, especially that of Knowles after injecting adrenalin. The latter had succeeded only once in thirty-four attempts to make blood cultures where the blood smears had been positive. Dr. Young had not succeeded in getting any cultures from the general circulation.

Dr. Robertson gave a summary of the cases treated in the clinic with antimony compounds during the past year. Potassium and sodium antimony tartrate as well as the colloidal antimony trisulphide were used. It was stated at the outset that a fair estimate of the results of treatment could not be given on account of the difficulty encountered in inducing patients to continue treatment over a sufficient length of time. Of sixteen patients in whom treatment with antimony compounds was begun, only seven received a sufficient amount of the drug. Four of the seven showed complete disappearance of all evidence of the disease. Final observations were made two to nine months after treatment. In all these patients the disease had been present only a short time before treatment was begun. The remaining three all showed very marked improvement but still had enlarged spleens. These patients gave a history of splenomegaly for a year or more before coming to the hospital. It is possible that in certain patients with a long history of kala azar a moderate degree of permanent splenomegaly may persist after the disease is cured.

Dr. Korns reported on the experimental work with the different antimony compounds in rabbits and showed that potassium and sodium antimony tartrate and colloidal antimony trisulphide were all toxic beyond a definite dosage. There was no evidence that the colloidal antimony trisulphide was less toxic than the other drugs that have been in use previously, namely, sodium and potassium antimony tartrate. His experiments also showed that none of these antimony compounds can be given intramuscularly, because experimentally in every instance the injection was followed by the formation of sterile abscesses.

In a series of rabbits injected with antimony in these three forms over a period of four months, with a dosage equivalent to twice the maximum dose for a human being in proportion to the weight, all rabbits gained in weight. At autopsy one rabbit which had been given the potassium salt showed fatty changes in the liver,

but none of the others showed departure from the normal. It would seem from these findings that the human dosage, in the case of the sodium salt and the colloidal sulphide, might safely be increased by from 50 to 100 per cent.

Dr. Robertson spoke on the general treatment of kala azar, stating that blood transfusion had been found to be of much value in severe cases. In this hospital it has now become an essential part of the routine treatment in those cases with marked anemia. Two hundred to 300 cc. of blood is transfused in children, and 400 to 500 cc. in adults. For cancrum oris the practice has been to curette where there is a large amount of slough, then to apply 50 per cent silver nitrate locally. This has given good results in several cases. There were two cases out of a series of eighteen that developed an edema of the larynx and had to be intubated. In both these cases it was necessary to keep the tube in place for several weeks. They both made a good recovery.

Observations are being made on the effect of diet on recovery from the anemia of kala azar. This is based on the experimental work of Whipple and his co-workers, who found that dogs made anemic by bleeding and then kept on a purely carbohydrate diet showed a very slow blood regeneration or often none at all; whereas if such anemic dogs were put on a diet consisting largely of meat, recovery took place rapidly. Cooked liver was even more effective than meat. We are now adding to the diet of all kala azar patients a liberal amount of cooked liver. Recovery from the anemia of kala azar is a very slow process, hence any decidedly favorable effect which this diet may exert should become easily apparent.

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Bacteriological Laboratory of the Associate Professor, Department of Medicine

Professor's Chemical Laboratory, Department of Medicine

ELECTROCARDIOGRAPHY

Dr. Franklin C. McLean demonstrated the electrocardiograph, including the taking of tracings.

The three leads and their significance were briefly discussed. The main points emphasized were : (*a*) that the electrocardiograph shows the mechanism of each heart beat; (*b*) that it is through the studies in electrocardiography that recognition of the arythmias was made possible, although the usual arythmias can now be diagnosed clinically without the use of the electrocardiograph.

A series of slides was then shown, comprising the main abnormalities found in clinical work.

Slide 1. Normal electrocardiogram showing the normal auricular and ventricular complexes.

Slides 2 and 3. Auricular extrasystoles. Normally, impulse in the auricle arises from the sino-auricular node, but in abnormal cases the impulse may arise from any abnormal focus in the auricle, producing the condition known as auricular extrasystoles.

In this connection it is to be noted that the premature auricular contraction is followed by a normal ventricular response, and this by a long pause.

Slide 4. Nodal rhythm.

Slide 5. Tachycardia. Rapid but normal auricular and ventricular complexes.

Slide 6. Ventricular extrasystoles. This is most common among the premature contractions. There is a premature contraction arising in the ventricle and followed by a compensatory pause.

Slide 7. Paroxysm of ventricular tachycardia.

Slide 8. Sinus irregularity. This is normal in dogs and is of little clinical importance in man.

Slide 9. Sino-auricular block. In this condition the impulse from the sinus fails to reach the auricle.

Slide 10. Incomplete auriculo-ventricular block. Occasionally auricular beats fail to produce ventricular response. Atropin usually restores the normal rhythm in this condition.

Slide 11. Complete auriculo-ventricular dissociation: auricle and ventricle contracting independently of each other. There is no time relationship between the auricular and ventricular complexes.

Slide 12. Prolonged conduction time.

Slide 13. Auricular fibrillation. Most common. There is a continuous fibrillation of the muscular fibers of the auricle, each contracts independently of the other.

This condition once established usually lasts throughout life, except for the transitory forms often observed in cases of acute lobar pneumonia. It is in auricular fibrillation that digitalis does the most good. Recent reports of German investigators have given good results with the use of quinidine, normal rhythm being restored by its use. This drug is, however, still in the experimental stage.

Slide 14. Auricular flutter. Extremely rapid auricular contractions with various grades of heart block. With the administration of digitalis, it may pass on to fibrillation, then the restoration of normal rhythm takes place when digitalis is stopped.

Slide 15. Mitral stenosis.

CONFERENCE ON LEPROSY

PARTICIPANTS:

DR. VICTOR G. HEISER
MISS RUTH A. WOOD
DR. R. M. WILSON

DR. HEISER gave a brief résume of the use of chaulmoogra oil in the treatment of leprosy. This oil has been used by mouth for many years by natives of the countries where the oil is produced, and has always been supposed to have curative properties. On account of the fact that few individuals can tolerate the oil by mouth for a sufficiently long time to produce a cure, its use was not very effective, until other methods of administration were tried. While in the Philippines, Dr. Heiser developed a formula for administering the oil intramuscularly, and was able to produce beneficial results in a considerable proportion of cases. At his suggestion the problem of isolating and purifying the active principles of the oil was taken up by Sir Leonard Rogers, who prepared the sodium salts and the ethyl esters of the fatty acids of chaulmoogra oil, and found that the therapeutic results were improved and the toxicity and unpleasant effects of administration were lessened. This work is being continued by Sir Leonard Rogers and by Dr. A. L. Dean of Honolulu who has improved the method of preparation of the ethyl esters and is also preparing other derivatives of the oil. Dr. Heiser has recently had an opportunity of observing the results of treatment with the newer preparations, and he estimates that about 50 per cent of cases of leprosy can be cured by the methods now available. Dr. Heiser questions the wisdom of spending large sums of money for isolating lepers and believes that better results will be obtained by spending the money on the treatment of cases in hospitals or in the homes of the patients. There are about six thousand cases of leprosy in the Philippines, all on one island, and the Bureau of Science is preparing to manufacture the ethyl esters of chaulmoogra oil in large quantities for the treatment of all cases.

MISS WOOD, formerly a chemist in Dr. Dean's laboratory in Honolulu, and now in the chemical laboratory of the Department of Medicine of the Peking Union Medical College, gave a brief description of the chemistry of chaulmoogra and other oils used in the treatment of leprosy. She described the process by which Dr. Dean prepares the ethyl esters of chaulmoogra oil, and gave some indication of the direction in which his present researches are leading him.

DR. WILSON, of the Kwangju Leper Home, Kwangju, Korea, described the results obtained by him in the treatment of leprosy by the Heiser formula, slightly modified (1 per cent of camphor in chaulmoogra oil). Dr. Wilson gives about 6 cc. of this mixture intramuscularly once a week, until cure is effected. He believes that the treatment will be improved by the use of the ethyl esters, but he has had such encouraging results with the present method that he believes it should be used until the newer method becomes more generally available.

Dr. Wilson discussed the sources of the oil. He obtains it from Japanese sources Chobei Takeda, Doshomachi, Kobe, Japan) at about two yen per pound. This

oil is likely to be adulterated, but has given good results in his hands. He also obtained oil from Calcutta (Smith Stanistreet).

There followed a general discussion of the leprosy problem, in which the following points were brought out:

1. There are probably about five hundred thousand lepers in China.
2. For the great majority of these cases, no treatment is at present available.
3. Ethyl esters of chaulmoogra oil are at present either unobtainable, or are too expensive for general use when obtained from commercial sources.
4. Until ethyl esters are obtainable, the chaulmoogra oil itself should be used for treatment, 4 to 6 cc. of chaulmoogra oil with 1 per cent camphor should be given intramuscularly weekly.
5. Dr. Heiser will endeavor to learn whether the Philippine government will supply the ethyl esters to physicians in China at cost price, and this information will be given out by the Department of Medicine of the Peking Union Medical College.
6. The Peking Union Medical College can be of service to physicians in China in the following ways: (*a*) by disseminating information as to the value of preparations, as to sources of supply of chaulmoogra oil and its derivatives, as to methods to be employed in the treatment of leprosy; (*b*) by investigating methods for the detection of adulterants of chaulmoogra oil; (*c*) by investigating the possibility of substituting other oils, native to China, for chaulmoogra oil in the treatment of leprosy.

CONFERENCE ON SPRUE

PARTICIPANTS:

DR. H. JOCELYN SMYLY
DR. J. B. GRANT
DR. E. W. EWERS
DR. RALPH G. MILLS
DR. R. M. WILSON
DR. SAMUEL COCHRAN

DR. GRANT reported first hand observation of the work of Dr. Bailey K. Ashford in Porto Rico. Ashford in 1914 claimed to have isolated from tongue scrapings and stools of sprue cases an organism which he thought to be the causative agent of sprue. This organism was also found in mouldy bread. With his associates, Ashford developed a vaccine treatment, which they first claimed to be curative in 100 per cent of cases. Dr. Grant observed one of their cases during treatment over a period of six months. This was a severe case, treated with an autogenous vaccine. After a month of weekly injections the sprue stools cleared up, but the stools did not become normal. There was no further improvement after three months more of treatment and Ashford finally gave up this case. In every patient seen by Dr. Grant the results were the same, the sprue stools cleared up, but there was not complete cure.

Dr. Grant's opinion is that sprue is due to dietary deficiency with a secondary infection. He does not believe that Ashford's vaccine will cure sprue, although it is of benefit in clearing up the stools. Dr. Grant referred to an article by Dr. Trevor B. Heaton (1) in which the conclusion is reached that sprue is due to a physiological deficiency of ferments.

DR. EWERS stated that sprue is common in all parts of China. In South China he said most cases are in pregnant foreign women, in Central China in single foreign women, most of whom were on their second term in China. He has seen only one case in a Chinese, working in a foreign drug store. He has seen no cases cured. Fat-free milk, given in quantities of about 5 liters a day will quickly stop the intestinal symptoms, but will not cure the disease. Dr. Ewers stated that some of the common symptoms, in addition to the tongue and gastro-intestinal symptoms, are changes in disposition of the patient, increasing irritability, shortening of memory, and tetany. In the terminal stages the liver is very small, there is an advanced degree of emaciation, and the skin is yellow.

Dr. Ewers said that he had heard recently from Dr. Ashford, who now suspects that the pancreas is at the root of the condition, and that Dr. Ashford is now giving 1 gram of pancreatin with every feeding.

DR. MILLS described an autopsy on a case of sprue, in which he found extreme emaciation and atrophy of the mucosa of the intestines. The pancreas was small but no structural changes were found.

DR. WILSON stated that there are about twenty-five cases of sprue in Korea, among about seventy-five missionaries. Dr. Wilson believes that the tongue symptoms, and gas and pain in the abdomen are early symptoms, and that diarrhœa

comes later. He has seen no cases in Koreans. He has used buttermilk with benefit, and advised giving fruit.

Dr. Cochran suggested that the etiology is from bread made with contaminated yeast cultures, and suggested that particular attention be paid to this. He stated that soy-bean products are valuable in the diet.

DISCUSSION

There followed a general discussion in which the following points were brought out:

1. Sprue is common among foreigners residing in China and Korea, especially among missionaries, but either does not occur, or is very rare, among Chinese and Koreans. It is more common among foreigners who have resided for a long time in the Orient, and has not been observed in individuals who have lived in China for less than one year.

2. It is either incurable, with present methods, or practically so, and runs a chronic course of long duration, usually terminating fatally.

3. The vaccine treatment of Ashford and his collaborators is of some benefit, but is not curative.

4. An exclusively milk diet, preferably of fat-free milk, is of the greatest benefit in alleviating the symptoms. Buttermilk, soy-bean products, and fruit are of value in the diet.

5. Medication, with the exception of alkalis, which help the tongue symptoms, is of no value.

6. Cases are as a rule better treated on the field, where the medical profession is experienced in the treatment of the disease, than by sending them back to America or England.

7. Studies of diet in relation to the cause of the disease, of pancreatic function, and of contamination of food supplies, particularly of bread, are most likely to give information of benefit in combating the spread of the disease.

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TUBERCULOSIS

By

John H. Korns, M. D.

A. PROPHYLAXIS

1. Source of Infection

Because of its bearing on prophylaxis we are interested here in China in the incidence of infection of man with the bovine type of the tubercle bacillus. Does this type of infection occur in China? According to Kitasato it does not occur in Japan, and conditions are similar here in China. That is, cows' milk is little used, beef is little eaten. I am anxious that those of you in North China who are removing tuberculous glands from children under fourteen years of age, send me the fresh glands for injection. The rabbit I pass around, which was autopsied this morning, was injected intravenously July 22 with 0.01 mg. of virulent bovine tubercle bacilli. After running a febrile temperature and losing 450 grams weight, it has succumbed. You see the lungs are studded throughout with small yellowish nodular masses; the liver and kidneys also show tubercles. These areas under the microscope show numerous tubercle bacilli.

On the same date (July 22) another rabbit was similarly injected with human tubercle bacilli. This rabbit has gained in weight and is afebrile.

This illustrates the relatively greater susceptibility of the rabbit to the bovine strain, and establishes, therefore, one means of differentiation.

Besides cattle as a possible source of bovine infection in China, we must think of hogs. Hogs are numerous, are in rather close contact — if not directly, at least through their excreta and through flies — with the food of children in China. We are ignorant of the incidence of swine tuberculosis in China, but if it in any degree approaches the incidence in the United States, this factor must be considered.

The estimate of Rogers, based on packing house inspections, is that there are ten million tuberculous hogs in the United States. In China, however, the greatest menace is the open human cases of pulmonary tuberculosis. I think we are safe in assuming this; and while we may be unable in our clinics materially to affect advanced open tuberculosis, yet if we can make patients thus affected harmless to the community by properly caring for their sputum we are doing a good work. Supposing one patient expectorates twenty billion organisms a day, it is extremely important that this source of infection be eliminated.

2. Childhood Infection and Reinfection

You are familiar no doubt with figures collected in other countries with regard to the high incidence of childhood infection. Hamburger, in Vienna, showed that by the time the fourteenth year of age has been reached 94 per cent respond positively to the von Pirquet test. In New York, Park found at this age 75 per cent. It is altogether likely that in China, a highly "tubercularized" nation, a similar high incidence occurs. Now if children are practically all infected, is there danger later in life from reinfection? Is it sufficient for us to direct all our prophylactic measures toward protecting children?

On examining the literature one finds that there are diverse views with regard to the possibility and common occurrence of reinfection. Bushnell (1) says reinfection cannot occur after a preliminary infection has been established. A patient with pulmonary tuberculosis will preserve his immunity to the end of his life. Cornet, von Behring, Hamburger, and Römer adhere to similar views.

Adami (2) holds that the relative rarity of the bovine type in adults demands one of three views:

1. That the bovine infection acquired in childhood is peculiarly fatal so that all persons affected die in their early years (and this has no support in fact);
2. That in many cases it dies out and is replaced later by infection with the human type (and there is no clear proof of this);
3. That gradually through long residence in a human host the bovine form takes on the character of the human strain. The fact that we occasionally find intermediate strains seems to favor this third view. But some would say in reply to the third alternative that these so-called intermediate strains are really mixed cultures, containing both human and bovine strains.

On the opposite side of the fence are men like Theobald Smith who thinks the tubercle bacillus coming to the lungs from without has as good a chance as one carried there from a pre-existing focus. Smith has shown in experimental work that it is the size of the reinfecting dose which is important.

Krause thinks reinfection possible, hence the importance of environment.

Calmette believes reinfection occurs, the adult consumptive being one who has received since childhood successive more or less massive reinfections.

In the face of these views upholding the possibility of reinfection, as well as in the face of our own clinical experience, we are not justified, therefore, in limiting our prophylactic work to children. Nevertheless, we in China should stress efforts to protect children from repeated massive infections, separate babies from tuberculous mothers and amahs, and teach the means of transmission of the disease most likely and most preventable in the homes.

B. EARLY DIAGNOSIS

One of the most discouraging features of tuberculosis work in China is the enormous percentage of advanced cases which come for treatment. Those of you who in mission stations or elsewhere act in the capacity of health officers do, however, have the opportunity to detect early cases and should be prepared to do it. We are struck with the large numbers of students of the asthenic type, and I want Dr. Willner, who is in charge of student and staff health here, to speak briefly about his observations and measurements. (Dr. Willner described the Becker-Lennhoff index and Korányi's sign.)

Those of you who have access to the Roentgen rays will agree with me that this method of diagnosis is of great value in many early cases showing no physical signs or only equivocal ones. (Four cases were shown to illustrate the value of the X-ray both in detecting early tuberculosis of the lungs and in following the course of the disease. Films taken at six-month or nine-month intervals were also demonstrated. In connection with one, a case of hilus tuberculosis, the value of D'Espine's sign was emphasized.)

Some of you are so situated that you cannot use the X-ray in routine work.

You will agree that if we had some specific test for active tuberculosis that is simple in its technique and interpretation all of us would be greatly delighted. In 1919 Wildbolz described his auto-urine test which he claimed was specific. This has been confirmed by Imhof, Gramen, and Alexander. One of the best discussions I have seen, together with confirmatory tests, is by Gibson and Carroll (3). (The theory and technique of this test are described.)

While our own experience is too brief to be certain of the specificity and value of this test, the results of others suggest it to be of distinct use.

C. CHEMOTHERAPY

Our conference on the treatment of leprosy day before yesterday was valuable and showed that rapid progress has been made recently. Are we too sanguine in expecting similar progress in the treatment of tuberculosis? I had expected Dr. Shiga to talk on the chemical treatment of tuberculosis, but he was obliged to leave the city this morning. The literature on this subject is extensive and in the time remaining I shall touch only upon the work initiated by Sir Leonard Rogers and carried on by his colleagues in India. Rogers thought he had found sodium morrhuate to be helpful in leprosy and so was led to conclude that there is nothing specific against the leprosy bacillus in the chaulmoogra oil series. Naturally, it occurred to him that in tuberculosis, another disease caused by an acid-fast bacillus, the fatty acids of these oils might be efficacious. First reports upon the use of sodium morrhuate in tuberculosis were very encouraging.

Other workers in the United States have had negative results, and now Rogers (4) himself confesses that neither the morrhuates nor the chaulmoogrates have been able to influence the course of tuberculosis in rabbits and goats. Walker and Sweeney showed both to be bactericidal to the tubercle bacillus *in vitro*. Here again we see the danger of drawing too many inferences from successful test-tube experiments.

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DEPARTMENT OF GENERAL SURGERY

OPERATIVE CLINIC: RADICAL CURE OF INGUINAL HERNIA

By

Adrian S. Taylor, M. D.

The operative procedure was as follows: The skin was prepared by painting with 5 per cent tincture of iodine. An oblique incision was made above Poupart's ligament, beginning above 1 cm. medial to the anterior superior spine of the ilium and ending 1 cm. lateral to the pubic spine below. The aponeurosis was split, the superficial ring opened, and the aponeurosis reflected upward to the edge of the rectus and downward to Poupart's ligament. The cremaster muscle and fascia were divided longitudially along the cord, and the sac at once opened. With the finger within the sac, it was separated from the cord by sharp dissection. Its neck was isolated, and after inspection of its interior it was twisted and the neck transfixed at its highest point and tied with medium silk. The sac was then cut off, and the stump was seen to retract well beneath the internal oblique.

Without disturbing the cord, closure was done as follows. The cremaster muscle was draw in under the internal oblique and sutured up under this muscle with mattress sutures of fine silk. The edge of the internal oblique, with the conjoined tendon, was sutured to Poupart's ligament. Interrupted sutures of medium silk were used. The cut edges of the aponeurosis were overlapped and sutured with silk. Scarpa's fascia and the skin were closed separately with interrupted sutures of fine silk. A dry gauze dressing was applied.

In the course of the operation, Dr. Taylor made the following remarks: The anterior superior spine of the ilium and the spine of the pubis are first identified, and the incision made through the skin, beginning above, medial to the first and ending below, lateral to the second. The aponeurosis is first opened above the ring and the incision carried down into the ring. Here one sees the ilio-hypogastric and the ilio-inguinal nerves lying beneath the aponeurosis. They are to be protected from injury. The cremaster muscle in this child is not well developed; it is incised along the cord and the large sac, which we see here, is opened. We were sure from our examination before operation that this was not a congenital hernia. This is verified by the ease with which the sac is separated from the cord. Now we have exposed the vas. This must be preserved, and here we may use a little gauze dissection, although we greatly prefer the sharp scalpel to rubbing with gauze. The sac is now free, and we isolate its neck above. Here the cord leaves the sac, and isolation of the neck is usually very easy. There is little danger of injury to the bladder in cases of this kind, while in direct hernia there is great danger in cutting or transfixing tissue lying outside the sac about its neck. We now inspect the interior of the sac and while watching the neck inside, we gently twist. It is now transfixed with fine silk, and as the assistant relaxes by untwisting, the neck is tied. The interior is again inspected, and being empty, the sac is cut off close to the suture. The stump is now allowed to retract, as you see, beneath the edge of the internal oblique muscle.

The first step in the repair was suggested by Dr. W. S. Halsted of Baltimore many years ago. I have here the cremaster muscle, which I will draw under the

edge of the internal oblique muscle in this way. You notice that I place the fine silk mattress sutures through the internal oblique well up on the face of the muscle. These sutures will catch the edge of the cremaster and draw it up beneath the internal oblique. As I tie these sutures, you notice how they roll out and make very prominent the edge of the internal oblique. These sutures also relax the muscle and bring its lower edge closer to Poupart's ligament, and undoubtedly relieve the tension on the sutures to be placed next.

The edge of the muscle and conjoined tendon is now approximated to Poupart's ligament with interrupted silk sutures. You notice how I place the lowest suture, attempting to include a bit of Gimbernat's ligament. This suture when tied approximates the structures closely about the cord at the pubic spine. There is little danger of constriction of the cord here. The lower cut edge of the aponeurosis is now to be drawn up on the internal oblique and sutured in place. The upper edge is drawn down over the lower and overlapped. All vessels will now be tied with fine silk. The wound is now perfectly dry. We feel that complete hemostasis is very important, and we tie every bleeding point with fine silk. The edges of Scarpa's fascia are now brought together with fine silk, and the skin closed likewise with interrupted sutures of fine silk.

I consider silk far superior to catgut for this operation. We do not use large strands. The strain is evenly distributed over many interrupted sutures, carefully tied, and we believe that there is less cellular reaction about these sutures than about catgut. Infection in our hernia wounds almost never occurs, and we have had no experience with sinuses leading down to the silk sutures. After infection there is recurrence in 50 per cent of cases. In children, without infection, cure is certain in practically all cases. In patients of all ages with indirect hernias, one may expect recurrence in about 5 per cent. In direct hernias the percentage of recurrence will be very close to 20 per cent.

A second case of the same condition was operated upon. The procedure and the surgeon's observations were the same as in the first case.

Corridor of the Out-Patient Department

One of the Four Main Operating Rooms, Fourth Floor of the Dispensary and Hospital Laboratory Building

DEMONSTRATION: BALKAN FRAME AND APPARATUS FOR THE TREATMENT OF FRACTURES

By

George W. Van Gorder, M. D.

From the casualties of the recent war, we have learned a great many lessons, and one of the most important of these, surgically speaking, has been derived from the treatment of fractures. Not only has our knowledge of bone repair and injured joint function been greatly increased, but remarkable improvement has been effected in the methods of handling fractures to insure the best end results. Progress in this latter direction was due largely to the introduction and invention of certain kinds of surgical apparatus and splints.

In attributing the advance to the employment of new splints, I am aware of the fact that a splint *per se* is not fool-proof and may permit a hideous deformity unless used properly. It is the proper use of each splint that I now wish to infer, when speaking of their relative values. We all appreciate that it is the human element, the directing and manipulating hand of the surgeon, his thoroughness and strict attention to minute details concerning the fracture that has the most to do with its final good result.

But some splints and apparatus, we must agree, are more nearly fool-proof than others; some answer a greater number of requirements, some are more practical and adaptable. We must have in a splint the combined qualities of simplicity, adaptability, and proper mechanical principle; and the splints I shall discuss this morning will be, I think, of this character.

First in order of its importance I will mention the Thomas splint, which, although not a new device, was not, previous to the war, so keenly appreciated as it is now. After the introduction and universal use of this splint in the British Army for fractures of the femur it was estimated that the previous mortality resulting from these cases was reduced by more than one half. Certainly all surgeons who have used the Thomas splint properly must be impressed with its simplicity, adaptability, and effectiveness. In demonstrating its application and use this morning, I shall not discuss its general mechanical principles, which are known to all of you, but shall mention only a few points that are of practical value.

The first one is this — no matter what the size of the Thomas ring, if applied to the leg it must not ascend above the tuberosity of the ischium, but must impinge there and press against the tuberosity, if effective heavy traction on the leg is desired. Especially is this true in adult patients, who cannot stand heavy counterpressure against the ramus of the pubis or the perineum. If the ring is made to fit a patient's leg precisely, then it will naturally rest against the tuberosity, but if taken from a stock supply, as is the usual case, it may be excessively large and then will have to be held in place by being suspended from an overhead frame as illustrated by the case before you. Just enough weight is placed in the shot bag as the other end of the pulley rope to keep the ring continually in apposition with the posterior surface of the leg. Thus if the patient lifts his body in the middle, as, for example, in using a bed pan, the Thomas ring automatically

rises with him and is consequently not permitted to override the tuberosity. This idea of suspending the ring from above the body was first introduced, I believe, by Major Pearson of Edmonton, England, and its employment by him and many others has been rewarded by splendid results in the treatment of fractures of the femur. Without observance of this precaution, one can go so far as to say that no adequate traction can be obtained with comfort, especially if the patient is kept in a level position, and the value of the Thomas splint is, therefore, tremendously handicapped and sometimes nullified.

The second practical point I should like to mention is the employment of a subsidiary iron splint identical with the lower portion of the Thomas and attached to it by a movable joint at that point where the patient's knee joint rests. This is known as a knee flexion apparatus, because the lower leg resting upon it is thus allowed to move up and down, flexing the knee at the will of the patient, who controls the movements by means of a pulley rope, as seen here. In any cases of traction employed above the knee joint, as in the use of ice-tong calipers, this knee flexion apparatus can be applied and thus prevent the knee joint from becoming stiffened from disuse. In all fractures of the femur where union has already begun to take place, this accessory splint can be of great help in restoring early function to the knee joint. This procedure also originated, I am informed, in the fracture femur clinic of Edmonton, England.

Another idea that is often of value in the use of the Thomas splint is to bend it, not at the knee joint, but at the site of the fracture, in such a way as to produce a convex anterior curve at a point just below the bone fragments. This is especially important in supracondylar and midshaft fractures, where the tendency for the bone fragments to sag is ever present. By thus arching the splint at a point just above the knee joint or in the midthigh, according to the site of the break, the bone fragments are lifted up and maintained in a proper position until union can take place.

For fresh fractures with much displacement, in addition to the ordinary force of traction, one can apply lateral pressure to the leg at any point by means of a so-called "femur pressure pad," which can be attached to the sidebars of the splint. Then by means of a turn-screw the pad can be driven against the leg as firmly as is necessary to correct the alinement, which is noted by successive bedside X-ray pictures.

The Thomas splint which you see applied here, the knee flexion apparatus, and the present pads were all made in China at a total cost of $3.00 Mex.

For compound fractures of the lower leg just above the ankle joint, where skin traction is out of the question and where a Sinclair skate is not strong enough to maintain a reduction of the deformity, we find the stirrup the most useful appliance in securing traction. It is simple to apply and, overriding the superior surface of the os calcis, as it should, does not produce an osteomyelitis as the Steinman and Hawley pins may do when driven through the bone itself.

In the treatment of fractures of the humerus, the two splints here demonstrated are of especial value. One of the straight arm Thomas splints with elbow flexion attachment is comfortable and effective for bedridden patients and its use has the advantage of preventing stiffness of the elbow, during the period of bone repair.

The other splint is the Jones arm splint, used for patients who are able to walk about. It is extremely useful for compound fractures in that dressings can be readily done without disturbing the support of the fracture.

The purpose of the conference this morning was more that of a demonstration of apparatus than a treatise on the subject of fractures. The various splints, braces, leg pillions, and artificial arms which you see are those which we have found to be the most useful and practical, and which are constantly employed in this hospital.

SKIN GRAFTING — THIERSCH AND REVERDIN

PARTICIPANTS:

DR. GEORGE Y. CHAR
DR. ADRIAN S. TAYLOR

Notes on the demonstration and discussion follow: The use of Dakin's solution in infected wounds has greatly increased the scope of skin grafting. Granulations growing up firm and red with a minimum of exudate offer an excellent ground for the transplantation of either large or small grafts.

The large Thiersch grafts may be taken from the anterior surface of the thigh, as large as a person's hand. The sides of the thigh are supported by sand bags. The skin is stretched between the edges of two boards pressed against it. The graft may be cut as long as desired and as wide as the thigh permits of flattening.

Reverdin "pinch grafts" are very satisfactorily made under local anesthesia. This method was demonstrated by Dr. Char. The external cutaneous and anterior crural nerves are blocked with novocaine. The grafts are taken by picking up the skin with the point of a needle held in an artery clamp. The top of the little hillock thus formed is cut off. The grafts measure about 5 by 12 mm. and are then transferred to the new field and pressed firmly against the bare surface. Several hundred may thus be transplanted, leaving spaces of 5 mm. between the islands. The thigh is then dressed with vaseline gauze. The grafted area is allowed to dry for eight to ten hours and then a gauze compress soaked in Dakin's solution is applied and changed every two hours for four days. After that a Carrel tube may be used over the gauze and the gauze changed every twenty-four hours.

An important point to be remembered is that after planting the graft the needle and artery clamp must be reboiled before being used again, in order to avoid contaminating the thigh wound.

EPITHELIOMA

By

FRANK MELENEY, M. D.

INTRODUCTION

I should like to review with you this morning some of the recent literature on epithelioma and give a brief description of the various forms. Dr. Tuffier and Dr. Taylor will discuss the surgical aspects, with special reference to two cases we have recently had in the hospital, and then we will use the microscope to show the various features of epitheliomata which have been described in the recent literature. Almost all of the special characteristics of epithelioma are shown under the microscope this morning, — curiously enough, I think, because we have had only twenty-three cases in the past fifteen months.

The nomenclature is gradually becoming more and more clarified, so that when an epithelioma is spoken of, it now means just one thing, — a malignant tumor of squamous epithelium, — leaving the term carcinoma for a malignant tumor of other forms of epithelium. In spite of the fact that at the present time we know very little about cancer, it is surprising, in looking over the literature, to find the authorities speaking with unanimity of the cause of cancer. Paine, director of the Cancer Research Institute in London, believes that cancer is not a specific disease due to a special parasite, but that it is a disorderly growth of epithelium, due to chemical or physical irritants, of which the toxins of bacteria are the most important. Ewing, in his textbook on neoplastic diseases, in speaking of epithelioma, says that he believes that in almost every case the disease is due to chronic traumatism. He says that it arises from normal epithelium after a period of overnutrition and overgrowth, during which the subepithelial tissues show some changes which make them less resistant to the down growth of epithelium. Those changes are lymphatic infiltration, mucoid or other forms of degeneration, atrophy of elastic tissue, fibrosis and chronic edema; and they usually, but not always, precede the down growth of epithelium. He says we must consider that normal epithelium has the power of becoming malignant if the proper conditions are brought about, but that there must be inherent in the epithelial cell itself some controlling influence which makes it grow outside of its normal limits. Broders and MacCarty, who are pathologists at the Mayo Clinic, believe that chronic degeneration of any specific tissue results in pathological, histological, and clinical changes in that tissue. The histological changes are hyperplasia, hypertrophy, and migration of the cells. The biological changes are hyperactivity and regeneration, and the clinical changes are either malignancy or benignancy. Broders, who has very extensively summarized the material from the Mayo Clinic, believes that cancer is not a degenerative process but a regenerative process; that the cells regenerate in response to an irritation; but that not only do they have the power of regeneration but also have the power of invasion and migration. Whereas the regenerative qualities are helpful to the normal body, the invasion and migration of these cells has a harmful effect.

It is interesting, I think, that these four authors who have written recently on epithelioma are so alike in their impression that irritation is the most striking cause. What evidence have we of the possible truth of this theory? There is no definite proof as yet, but the fact that epithelioma develops in the exposed parts of the body, the parts that are constantly exposed to irritation, and also that there are certain specific occupational forms, is significant. Chimney sweeps and paraffin workers develop epithelioma in the thigh. In Africa a form of epithelioma called kangri cancer appears on the abdomen, and it has been demonstrated that the natives there cause frequent irritation to the abdomen by holding a hot stove against it, for warmth or for some other purpose. It is well known that epithelioma develops on top of chronic ulcers, chronic osteomyelitis with sinuses, burns and scars, on X-ray burns, on lupus vulgaris, on pimples, on eczema, and other chronic lesions of the skin. This is the clinical evidence which we have that irritation is the cause of epithelioma.

What statistical evidence have we? Broders, who has collected a large series of cases from the Mayo Clinic, has produced the figures shown in the following table, in his recent review of squamous-celled epithelioma of the skin, squamous-celled epithelioma of the lip, and basal-celled epithelioma. For our purposes I have combined some of the figures into a single brief table. (Table 1.)

TABLE I

Broders' Statistics

	Lip	Skin	Basal-Celled
Male predominating	49–1	4–1	3–2
Farmers	56 per cent	53 per cent	Predominate
Average age	57 years	59 years	56.7 years
History of injury or irritation	See below*	24 per cent	Irrelevant
Following other lesions	63 per cent	51 " "	37 per cent
Average duration before being seen	2.6 years	4.8 years	7 years
Location above clavicle	Lower lip, 96 per cent Upper " , 3.5 " "	78 per cent	96 per cent
*Of cases of epithelioma of the lip	80 per cent are smokers		
Of 500 normal individuals	80 " " " "		
Of epithelioma cases who are smokers	78 " " use the pipe		
Of normal individuals who are smokers	38 " " " " "		

The table gives us statistical evidence of the effect of irritation or other lesion as an antecedent to the malignant growth. The figures in regard to pipe smoking are particularly interesting. In the skin epitheliomata 24 per cent were found to have a history of injury, and 51 per cent had some other form of lesion preceding the tumor. Inasmuch as, in the history, the diagnosis is made by the patient, it is difficult to be certain, of course, whether there was actually a different lesion or whether it was a form of the epithelioma which the patient did not recognize as

such. In epitheliomata of the lip other forms of lesions, including ulcers, were found in 63 per cent. The same uncertainty holds here. In the basal-celled epitheliomata a history of injury was irrelevant, but previous lesions were found to have been present in 37 per cent.

We have, then, this clinical and statistical evidence that irritation may be the cause of epithelioma or cancer. It is obvious that this is much easier to demonstrate in epithelioma, which is a surface cancer, than it is in the deeper cancers, such as those of the breast, of the stomach, gall bladder, or liver. And it must be remembered that we have no real proof that irritation is the sole cause.

Of the various classifications of epitheliomata that have been suggested, Broders and MacCarty's is the most complete and satisfactory. They consider (1) squamous-celled epithelioma, (2) basal-celled epithelioma, (3 and 4) pigmented and non-pigmented melanotic epithelioma, (5) adamantinoma, and (6) a mixed type of squamous and cylindrical tumor.

SQUAMOUS-CELLED EPITHELIOMA

The squamous-celled epithelioma is found wherever squamous epithelium occurs in the body — in other words, all over the skin, the mucous membrane of the mouth, down the esophagus to the stomach, the mucous membrane of the penis, the vagina, the cervix of the uterus, and the anus. It is also found where transitional epithelium occurs and in certain other places where normal squamous epithelium does not exist — in the lungs, in the bronchi, in the trachea, and in the gall bladder, which have cuboidal or columnar epithelium. This fact brings out a question in regard to the origin of squamous-celled epithelioma. Does it come from the normal squamous epithelium or from embryonal cell rests, composed of cells which are destined to become squamous epithelium but which are misplaced? Some men consider one origin more likely and some another. Adami and Ewing believe that normal squamous epithelium is always the source of surface squamous-celled epithelioma, and in those places where columnar epithelium is normally found it may actually change over into malignant squamous epithelium. MacCallum, on the other hand, suggests that those epitheliomata found in places where normally squamous epithelium does not occur arise from embryonal rests, which exist from the time the embryo is formed, and under certain conditions start to grow. This means that the rest must lie dormant for fifty or sixty years in some cases. On the other hand, there seems to be evidence that cylindrical epithelium can change into squamous epithelium. If there is complete inversion of the uterus, the exposed surface may develop squamous epithelium. The same is true if there is a complete prolapse of the rectum. So it may be also for the lungs, gall bladder, and other regions from some other form of irritation.

Adami and McCrae say that serial sections have shown that a squamous-celled epithelioma may have more than one point of origin. Ewing believes that this and other cancers may have several foci of origin, which later fuse, and that as they grow they extend in part by the gradual transformation of previously normal cells. MacCallum and others are of the opinion that malignancy begins at one point and spreads in all directions, pushing aside the normal epithelium but not actually changing the normal into the abnormal. Kilgore's recent study lends weight to this opinion.

Squamous-celled epithelioma may appear grossly in a number of different forms. It may appear as a papillary growth which is raised above the surface of the surrounding structures; it may appear as a cauliflower-like growth; it may be flat, and level with the skin, with simply a small raised margin, or it may be depressed and ulcerated. It may be soft or it may be indurated.

The microscopic appearance of squamous-celled epithelioma is most interesting. We know that the normal epithelium of the skin is bounded by a very definite basement membrane. In the upper layer we have the keratinized dead cells, then the stratum lucidum, then the prickle cell layer, and at the deepest part the basal cells and the basement membrane. The basal cells are cuboid or columnar. They are dark-staining and have round nuclei, with very little cytoplasm. The cells of the prickle layer have a considerable amount of cytoplasm and tend to take a squamous form, and their nuclei are pale. The most striking change which occurs in squamous-celled epithelioma is that the basement membrane, which normally is very definite, is lost. It becomes indistinct or absent altogether. The epithelial cells seem to be tumbling down from the surface like water over a dam. They grow wildly without restraint. There may also be seen the changes in the subepithelial tissues which Ewing describes — lymphocytic infiltration, edema, mucoid degeneration, fibrosis. Secondly there is evidence of rapid growth. Mitotic figures are found — one in every three or four high power fields, or sometimes several in a single field. Thirdly the cells themselves become abnormal. Broders has brought out a very interesting point in this regard. He has divided squamous-celled epitheliomata into groups, according to the degree of abnormality of the cell. He uses the terms "differentiated" and "undifferentiated." A differentiated cell is one which is like the normal adult squamous cell; the undifferentiated cell is supposed to have more primitive characteristics. It may look like a sarcoma cell; it may look like an embryonal cell. Let us consider this point for a moment. Kettle in his article on the polymorphism of the malignant epithelial cell says, "Everyone recognizes that the epithelial cell is capable of polymorphism, but without going so far as to say that the adult epithelial cell can actually become changed into a connective tissue cell, I am convinced that some carcinomata may possess such extreme power of polymorphic growth that their cells, losing all trace of their epithelial origin, may become indistinguishable from connective tissue elements." The differentiated type tends to form pearls. A pearl is a group of squamous cells which have gone on to keratinization. Broders says that pearls and the cells immediately around them are not cancer cells because they have become adult squamous epithelial cells and have lost the power of growth. I believe, however, that his statement is misleading. I agree that those cells have lost their power of growth, because they are dead, but it is certain that they were once cancer cells. If a pearl is found in a lymph node, for instance, one must say that the cells which formed it are cancer cells, because they had the power to leave the normal epithelium and invade the lymph node. Likewise if epithelium dips down into the deeper tissues as a malignant growth and later the cells go on their way to the adult form and become keratinized, a pearl is formed from cancer cells.

The epithelial pearl is one of the striking features of squamous-celled epithelioma, but there are squamous-celled epitheliomata without pearl formation. In the less differentiated type of growth fewer pearls are formed. The cells do not grow to

the point of keratinization. In the different grades of epithelioma we have all degrees of differentiation, from the embryonal cell to the epithelial pearl. If there is complete differentiation the epithelium is normal. If the cells are one-fourth undifferentiated, Broders classifies the tumor in Group 1. If there are equal portions of undifferentiated and differentiated cells he places it in Group 2. If three-fourths are undifferentiated he places it in Group 3. If all the cells are undifferentiated he classifies the tumor in Group 4. Broders claims that he can make a very definite prognosis from his grouping, quite independent of the clinical history and the age of the lesion. I believe that a more exact prognosis could be made if the age of the lesion were also considered. For instance, a Group 3 case developing in two months would be more rapidly fatal than one which had existed for two years. But this may be drawing too fine a point.

The following table gives Broders' statistics, indicating the incidence and the mortality in the four different groups five years following the best operation that could be performed in the case. The mortality percentage indicates the prognosis. There is a striking similarity between the two types. (Table 2.)

TABLE 2

Broders' Statistics

	Group 1	Group 2	Group 3	Group 4
	per cent	*per cent*	*per cent*	*per cent*
Lip incidence	15	62	21	1
Deaths	0	55	34	100
Skin incidence	8	69	17	5
Deaths	0	61	85	100

From these figures we may say that the more undifferentiated the cells are, the more malignant and the more fatal is the disease. A microscopic examination is obviously an invaluable aid to prognosis. I think that this classification should be followed up in more laboratories and hospitals, to see if these figures hold true elsewhere. This grading is the most significant work that has been done recently on epithelioma.

Among other changes which occur is the appearance of what is called the one-eye cell. This cell has a large oval nucleus, with a single, very densely-staining nucleolus. Some tumors show many of these cells, others few. Their significance is not apparent. Also the mitotic figures are very frequently abnormal in appearance. They are distorted into bizarre shapes and have not the regularity of development which is normally seen in the mitotic figure. There may be three or four distorted mitotic figures in a single cell.

What defense has the body against epithelioma? There is often a lymphocytic barrier between the epithelium and the deeper tissue. There are also endothelial leucocytes, which occasionally fuse to form giant cells. Also fibrous tissue seems at times to block off the growth of the epithelioma. But that is all the body can do. The outcome seems to depend upon the virulence of the cell rather than upon the resistance of the individual.

BASAL-CELLED EPITHELIOMA

The distribution of the basal-celled epithelioma is chiefly on the face. Ninety-six per cent of the cases are above the clavicle, and 90 per cent are above the line from the mouth to the mastoid. This is a very striking localization. Occasionally they appear in other parts of the body, in the deeper tissues and sometimes in the small intestine.

Krompecher, in 1900, was the first to describe carefully this form of tumor, which he said came from the basal cells of the epithelium — the cells which line the basement membrane. The cells of a basal-celled epithelioma, for some reason or other, have not the power to become adult squamous epithelial cells; they cannot develop keratin; they do not form epithelial pearls; they remain small and round or polygonal and are dark-staining. Borrman believed that they do not come from the basement membrane but from embryonal rests. This theory has grown out of the fact that in some cases basal-celled epitheliomata are found which seem to have no relation whatsoever to the surface epithelium but lie entirely beneath it. Janeway believed that these epitheliomata might come from either embryonal rests or normal epithelium. Ribbert was of the opinion that they all come from normal basement epithelium.

It is surprising that the basal-celled epitheliomata, which are composed of undifferentiated cells — young cells that have not the power to become adult cells — are less malignant than the squamous-celled epitheliomata. This paradox has not so far been explained. Here we have undifferentiated cells but the tumor is very benign. It lasts a long time without killing the patient; it almost never metastasizes and it can be relatively easily cured.

The gross appearance of the basal-celled epithelioma is often that of a nodule underneath the skin. It appears sometimes as a little sebaceous cyst or an adenoma; or it may appear as a persistent pimple; or as an ulcer which grows and does not show any tendency to heal, or tends to heal and then breaks out again; or it may appear as a scaly lesion with a coarse scabbing which forms and then rubs off. The basal-celled epithelioma spreads out laterally without penetrating very deep. It will go sometimes to the fascia and stop there. On section it may show a fairly definite limitation at the fascia. Or it may break through at one point and spread down to the muscle or bone and be checked there, and later break through the periosteum and get into the bone. When it occurs around the eye or nose or ear it may destroy large areas of the face and get into the sinuses.

Let us consider the microscopic appearance. The cells appear as small, dark-staining round cells, which do not show prickles; and although they may show enormous numbers of mitotic figures and grow very rapidly, the tumor is relatively benign. Instead of forming epithelial pearls the center of a cell mass will often show simply cellular débris. Sometimes these cell masses contain cyst-like cavities, and the tumors have often been diagnosed as alveolar sarcoma or endothelioma.

Going on to the other forms, I will run over them very briefly, because although they are important, they are relatively infrequent.

MELANOEPITHELIOMA

The origin of this type of growth is supposed to be the mole cell which lies immediately beneath the epithelium covering a mole. In the pigmented moles these

cells have pigment in and about them. It is a debated question whether these mole cells are really epithelium or connective tissue, and there has always been much discussion as to whether these tumors were melanosarcomata or melano-epitheliomata. The more recent opinion seems to be that they really have an epithelial origin. They may occur anywhere on the surface of the body; they are not often found inside the body, although other melanotic tumors do occur. Broders and MacCarty have divided these tumors into two classes — the non-pigmented and the pigmented. Sometimes the partial removal of a pigmented mole will start a melanoepithelioma, or it may start spontaneously. The gross appearance may show a large fungating mass of dark colored tissue or a small raised area resembling a blood blister, with the main mass of the tumor lying deep. On section one may find a single mass of black tissue, or there may be an unequal distribution of the pigment. Microscopically at the edge of the tumor one can generally observe the continuity with the normal epithelium, but the cells of the main tumor show very little differentiation. They very quickly lose the normal appearance of squamous epithelial cells and often resemble sarcoma cells. The cells are large and generally show many mitotic figures. One may see small areas packed with pigment and other areas with no pigment at all. The pigment may be within the cells or outside of the cells. It is a very malignant tumor, with 100 per cent mortality. It metastasizes very rapidly to the lymphatic glands, and may spread all over the body. It is curious that sometimes the metastases have no pigment at all, whereas the tumor itself is full of pigment, or vice versa.

ADAMANTINOMA

The adamantinoma is a tumor of squamous epithelium which apparently originates from the enamel organ at the root of a tooth. The gross appearance is that of a tumor which may become as large as an organ. It is more often found in the lower jaw than in the upper. It has a thin bony shell on the outside, and on section shows many cystic cavities filled with yellow degenerated material. Under the microscope it presents a very definite picture. It consists of masses of squamous epithelium, the outer or basal layer of which is very dark-staining. The nuclei are round or oval and the basement cells are cylindrical. Inside this layer the cells are first cuboidal and then squamous. In the center there is a degenerated area which may either be filled with cellular débris or may be empty, forming a cyst. They are relatively benign tumors, and if the gross tumor is removed, they do not recur.

MIXED TUMOR

Broders and MacCarty have also described a mixed tumor which occurs rather infrequently in the palate. This is a mixture of squamous and glandular tumor tissue, and is so relatively infrequent that I will simply mention its occurrence.

DISCUSSION OF SURGICAL ASPECTS OF EPITHELIOMA

PARTICIPANTS:

DR. THÉODORE TUFFIER
DR. ADRIAN S. TAYLOR

DR. TUFFIER: Dr. Taylor has asked me to examine this patient, a woman of middle age, who has never had a serious disease. She now has a tumor of the tongue in the posterior third, on the right side. It is only a little more red than the tongue itself. There has been very little pain, nor is it painful when I put my finger upon it. All the movements of the tongue are free and without pain. In this location on the tongue such a small tumor can be acute or chronic. This is chronic. One year ago the patient noticed a little pain in that part of the tongue. She consulted a dentist, who found one tooth that caused pain and removed it. The tumor did not disappear, but it has not enlarged.

We must know the diagnosis, the prognosis, and the treatment. I have seen three patients in my experience who had this kind of tumor. You all know that in such a position a very small lesion may be very painful. There are many patients who come and say that they have a bad tumor of the tongue which is very painful. You examine them and find nothing at all. They come again, and finally you find a small tumor which gives very great pain. In those cases the tumors are not really tumors; they represent an irritation of one very small part of the tongue, with great pain, and leave no bad results. I have also seen an adenoma of the tongue.

It is very unusual to see a cancer of the tongue in a woman. Such a diagnosis is very likely to be a mistake. When a woman is a smoker or syphilitic there is a cause of irritation; but in my experience I have seen only two cancers of the tongue in women. When Dr. Taylor told me his patient was a woman I immediately said, "Then probably it is not a cancer." This tumor has been in the same location and position for one year, and I have never known a cancer of the tongue to go on for one year without increasing in size. When you have a tumor going on for one year, in the same situation, without bleeding, without increasing in size, there is a great chance that it is not cancer.

This tumor appears to be hard but when you take it between two fingers it is not; it is elastic and can be moved very easily. Palpation proves that it is not a cancer..If you are in doubt as to cancer, what are you going to do? The tumor does not go deep but remains superficial, it is movable, elastic, and is not raised. With this condition present I believe the patient has an adenoma of the tongue and not a cancer. The prognosis really depends upon the surgeon. If you do not remove the cause of the chronic irritation or use a cautery, the condition may develop into cancer, as in other parts of the body. But without treatment it is probable that it will remain in the same situation for some years.

It is very difficult to say what is the best treatment for cancer of the tongue. When you use surgery you remove all the tumor. When you use X-ray you kill the cells in certain places. When you use radium you also kill the cells in certain places. I believe that a cancer of the tongue calls for radical treatment by surgery.

The first cause of cancer is a biological one. I believe, after an experience of

forty-five years, that very often the cure is partly medical — not entirely surgical. You must remove, if possible, the conditions that have caused the cancer. I think that radical treatment is indicated. If you could change the serum, or change the blood — if you could change the condition of the patient — you might arrive at a medical cure. But being unable to treat the condition medically we must do what we can for the patient by surgery, by X-ray, or radium. We do not know the cause of cancer of the tongue. I have operated on a great many cancers in my life, and I have had good results in some cases in which I have done the same operation that I have done in the case of patients who have died. It was certainly not because of my surgery, but because their condition was better. I have had four cases that recovered after fourteen years — why, I do not know — I did the same operation, the tumors were the same, and as large as the others. I believe that surgery is the best means we have; but even with surgery you cannot say that you will have a recovery.

I believe that in a cancer of the tongue the best thing to do it to remove all the glands above the clavicle at the first operation, and at the second operation to remove as much of the tongue as possible. But there is an element of uncertainty in the result.

In regard to the use of radium and X-ray, during ten years' experience I have seen radium used in many cases. There is a stage, in a small tumor of the tongue, in the deep part near the throat, when you can do better with radium than with the knife, because with the knife you can never remove very well all the tissues around the tongue. X-ray has given less definite results. The X-rays we were using about two years ago were not sufficient for recovery. I believe that the knife is the best after all, for it is very difficult to know the exact dosage of the X-rays. If you give too much X-ray it is possible to produce an irritation. (Irritation is perhaps the word. When we do not know what else to say we use the word irritation. But what is irritation? Is it a microbe? We do not know.) The same is true of radium, for you may cause a very bad condition of the tongue if you use radium in great quantities. In the presence of very extensive growths which I could not remove, I have tried radium. One patient was a physician with a very extensive ulceration of the tongue, who asked me to use all the radium we could. With the help of two of my friends I got tubes of all the radium we could find in Paris and put them in all parts around the tumor. This case was very curious and very disappointing. At first the patient seemed much better, but he developed symptoms of acute intoxication and died of intoxication coming from dead tissue. So, when we use a small quantity of radium we do not get good results, because it is not sufficient to kill the tumor cells; when we kill a large tumor at once by a large quantity of radium we have death from intoxication.

If this woman has a cancer of the tongue what is to be done for her? I believe it is best to remove the small tumor and to do a suture by first intention. The reason I say that an operation is the best thing in this case is because I think the tumor can be safely removed. I have not seen complications in such cases. And when you can remove such a tumor in the case of a woman who is fifty-one years old, and the operation is absolutely without danger, without risk, it is better to remove the tumor than to leave it. It is the same in many diseases. When you operate for appendicitis, you remove the appendix because it is less dangerous to remove

it than to leave it in place. In this case if the tumor is left, it is possible that after some months or some years the patient will have a cancer of the tongue. And so I believe that the best thing to do is to operate.

For a condition of the tongue that is very painful and without a tumor I think that cocainization is the best thing, and that the patient has more a tumor of the mind than of the tongue. Such patients are very often neurasthenic. In the case of an adenoma I believe that it is better to remove it than to leave it in place.

Dr. Taylor: I wish to emphasize a particular point, because we have had two cases along these lines recently. In the case of the patient whom you see this morning we received a letter and telegram from friends in Korea asking our advice, stating that the patient was a woman fifty years old, who had a small growth of the tongue. The advice we gave was to make a definite diagnosis and to be prepared to carry out the treatment required by that diagnosis, and not to take a section from the growth and send it to us for diagnosis. In the other case a small piece of tumor was sent to this institution for diagnosis. The tumor proved to be an epithelioma. We sent the report back and the patient immediately started for Peking. There was an interval of not over two or three weeks from the time the specimen was sent us until the patient arrived in Peking, but during that interval the growth had recurred *in situ* — that is, in the scar. A radical operation done at that time revealed metastasis in a lymph node along the internal jugular vein.

I should like to say a few words in regard to the type of anesthesia we use. A friend spoke to me the other day of etherization by rectum. I think this is justifiable if you cannot do better, but I believe that it is not the safest type of anesthesia for work around the mouth. We use the Connell ether machine, and we are able with it to regulate accurately the ether vapor tension. It has been found that if the proportion of ether mixture be kept constant, the depth of anesthesia is constant and regular. These machines are rather too complicated and expensive to be used in the ordinary mission hospital; they cost four or five hundred dollars gold. And then, too, such hospitals have not the necessary compressed air and electricity to run the machine. But one can improvise a very satisfactory ether machine with a glass bottle and rubber bulb. With ordinary satisfactory etherization, with the patient in the head-down position, the operation of the tongue is easily carried out.

Dr. Welch spoke to me a few minutes ago about the incidence of syphilis in these tumors of the tongue and also about the extreme rapidity of growth of carcinoma in the glands of the neck, and the poor prognosis, especially in cases with syphilis. In reading up these cases in recent literature, I found that very soon both sides of the neck become affected. One should, therefore, be prepared to clean out the glands on both sides of the neck, especially if the growth is in the posterior one-third of the tongue.

Now, if this tumor were malignant it would be in a very bad location. The prognosis is far worse for a growth in the posterior third of the tongue than for a growth in some other portion.

I have recently done the complete operation at one sitting, without difficulty. What is the danger of the complete operation? First, it is a major procedure. In the second place, there is the danger of infection. One does not try to save the

platysma muscle. Everything under the platysma muscle is removed *en bloc* by sharp dissection. The incision follows a crease in the neck, with a right-angled prolongation downwards. The platysma is not reflected with the skin, as in benign conditions of the neck. The skin alone is reflected, and the platysma excised at the limits of the wound. There are four groups of lymph glands — the submental glands, the submaxillary glands, the glands at the tip of the parotid, and the glands that go down along the jugular vein. Every surgeon has his own way of dissecting the neck. It is usually very easy to begin with the submental and the submaxillary glands and then to work backward to the glands at the tip of the mastoid. Of course here one must not cut the main branch of the facial nerve. It is perfectly justifiable to cut the third branch of the seventh nerve. As a matter of fact, I do not think that a radical operation can be done here and the third branch of the seventh nerve be saved. Then the jugular vein is dissected out. One may or may not save the vein. It is easy to dissect it safely, and in a radical dissection it is also justifiable to tie the vein low down and take it out with the mass of glands one removes. However, where one is going to do both sides of the neck it is not safe to take out the vein on both sides. With a sharp knife and careful, gentle dissection it is easy to strip the vein clean.

In the case done two weeks ago we did a radical operation at one sitting. The dissection of the neck went rapidly, without loss of blood. We excised the tongue at the same time, and the only complication we had was a very slight infection in the submaxillary region, where there was a light leakage of saliva for a few days.

The point I should like to make this morning is that one should not cut into these suspicious tumors of the tongue unless one be prepared to go the entire length and do a radical operation. The technique of frozen sections, which Dr. Meleney will demonstrate this morning, is available for everyone. One should make up his mind pretty definitely before he makes a frozen section as to the type of growth, and be prepared to do the radical operation or to do no operation at all.

THE PREPARATION AND USE OF DAKIN'S SOLUTION

PARTICIPANTS:

DR. ADRIAN S. TAYLOR
DR. THÉODORE TUFFIER

PREPARATION OF DAKIN'S SOLUTION

DR. TAYLOR: Dakin's solution is a solution in water of sodium hypochlorite ($NaOCl$) which contains not less than 0.4 per cent, nor more than 0.5 per cent, sodium hypochlorite, and which is not alkaline to powdered phenolphthalein but is alkaline to an alcoholic solution of phenolphthalein. If the percentage of sodium hypochlorite is less than 0.4 per cent, the antiseptic power of the solution is too low; if greater than 0.5 per cent the solution is too irritating. If the solution is alkaline to powdered phenolphthalein, the solution is irritating; if the solution is neutral or acid to an alcoholic solution of phenolphthalein, the solution is unstable.

The solution may be made in several ways: (1) from bleaching powder; (2) from chlorine gas and sodium carbonate; and (3) by electrolysis of a solution of sodium chloride. The first method, fully described in the literature, involves the determination of the chlorine content of the bleaching powder available, then the addition to a suspension of the bleaching powder in water of sodium carbonate. The amount used depends upon the chlorine content of the bleaching powder available. The reaction produces sodium hypochlorite and caustic alkali. This excess alkalinity is reduced in various ways. This method is rather unsatisfactory on the whole. From several cities in China word has come that bleaching powder of proper chlorine strength is not available.

The second method requires chlorine gas. This may be made locally in the usual way from common salt, sulphuric acid, and manganese dioxide, or it may be bought compressed in steel cylinders. Liquid chlorine gas is not made in China as far as we know, and as it is "deck cargo" it is expensive and difficult to obtain. The reaction between sodium carbonate and chlorine gas is a simple one, and the resulting product is the sodium hypochlorite desired. The amount of chlorine gas needed for a given amount of sodium carbonate to produce a solution of sodium hypochlorite of any desired strength is easily determined from the simple reaction involved. These figures are given in tables available in the literature. The gas itself is usually measured by means of a simple calibrated meter manufactured by Wallace and Tiernan Company, New York. The gas used may be actually weighed by blowing it through a solution of sodium carbonate in a tarred bottle, balanced on a scale.

In the third method a direct current of electricity of known strength is run through a known saline solution for a given time, and a solution of sodium hypochlorite in water of definite strength results. Cells for the electrolytic manufacture of Dakin's solution are on the market.

As the action of Dakin's solution depends on the chlorine content and on the alkalinity, determinations of both are necessary. The percentage of sodium hypochlorite is determined by titration with 0.1 N sodium thiosulphate, adding

potassium iodide and acetic acid to the Dakin's solution in order to give a visible index of the chlorine present. When potassium iodide is added to a solution of sodium hypochlorite in the presence of an acid, a double decomposition takes place, and free iodine is thrown down, one atom of iodine for each atom of chlorine present. The iodine thrown down is then easily determined by titrating with the 0.1 N sodium thiosulphate.

The degree of alkalinity must be exact, as a solution too alkaline will prove irritating to the tissues, while one too nearly neutral will be unstable. The ideal solution must give a definite pink reaction to an alcoholic solution of phenolphthalein, but must not give a color when the dry powder is added to it.

The action of Dakin's solution in a wound is two-fold. It has a bactericidal action, and is also definitely solvent for necrotic tissue in the wound. The bactericidal action depends upon the chlorine content; the solvent action depends upon the sodium hypochlorite and upon the alkalinity of the solution.

DEMONSTRATION

The preparation of Dakin's solution from liquid chlorine gas and sodium carbonate was shown. A specimen was examined and the percentage of sodium hypochlorite determined by titration. The alkalinity was tested, and was found to be between the end points for phenolphthalein, dry and in alcoholic solution.

USE OF DAKIN'S SOLUTION BY THE CARREL METHOD

Dr. Tuffier spoke of the introduction and use of Dakin's solution by the Carrel method during the war and its use in civil cases, particularly in empyema. He brought out the following points:

1. There must be contact with every part of the wound. If one part is not reached it will later be the source of reinfection for the whole wound.

2. Bacterial counts must be made every three or four days. Several parts of the cavity must be examined, because one part may become sterile and another part still hold its infection.

3. In those cavities where one cannot bring about contact of Dakin's solution with every part, an attempt must be made to alter the patient's serum in order to combat the disease. This may be done by either an autogenous or a stock vaccine; or by "proteinic shock." This is particularly important in bone or fat tissue infection.

4. The most important quality of Dakin's solution is its ability to dissolve dead tissue. Thus large quantities of bacteria are washed out, and sloughing tissue, which is the food for bacteria, is removed. This permits the body to destroy the bacteria with which the living tissue comes in contact.

DISCUSSION

In the general discussion other points were brought out as follows:

1. Wounds infected with streptococci are slower in becoming sterile than those where other organisms are present. For that reason cultures as well as bacterial counts are necessary. If streptococci are present the wound cannot be secondarily closed.

2. The granulation tissue which grows under Dakin's solution is red and firm

and flat. It does not tend to be exuberant. Skin grafts may be made upon it easily and successfully.

3. Dakin's solution can be used with benefit in tuberculous empyema but will not result in a closure. The patient gains in general health and strength. The same can be said of psoas abscess.

Dr. Tuffier: I will say just a few words about the use of Dakin's solution for the sterilization of wounds and of the cavity in empyema. In empyema we put the patient on his good side and wash out the cavity with the solution. That is very good in the beginning, but after twenty-five or twenty-six days vaccination is done. At the moment when the growth of the microbes ceases you can close the cavity. So for empyema you wash the large cavity with many tubes; and when the growth of the microbes, examined every three or four days, drops to one microbe per field under the microscope you can discontinue the Dakin's solution and close the cavity. The cavity is sterilized and the battle is won.

Where you have a very large cavity in the pleura and a bronchial fistula, you cannot use Dakin's solution, because the solution gets into the bronchus and the result is bad. In such cases you can do one of two things. Either before washing out the cavity the fistula may be plugged with a small piece of gauze, and when it is obliterated the cavity may be filled with Dakin's solution; or the patient may be turned on the bad side, so that when the cavity is irrigated, the solution will not get into the bronchus. You can do this in some instances, but with some fistulas you cannot use this solution. In those cases you can sterilize by oxygen. You do exactly the same thing as by the Carrel-Dakin method. You distribute through all parts of the cavity ten or twelve tubes, or even more. You pass a current of oxygen through all the tubes. That is sufficient for the disinfection of the cavity. The oxygen gets into the bronchus; you have no injury and no trouble for the patient.

These are the two methods. Certainly Dakin's solution is a very good solution for the disinfection of all cavities, but the great difficulty is to insert as many tubes as are necessary. If there is one part of the pleura where the solution does not reach you can be sure that the cavity will not be sterilized. The cavity may be sterilized save in a few deep inaccessible pockets. Search in these recesses with a long wire loop, with the cavity well illuminated, usually reveals sites of hidden infection. Tubes placed so as to reach such spots often lead to final and complete sterilization.

But this is only one condition. I have seen Dakin's solution used in numerous other wounds during the war; and it was certainly a very great blessing. And I have used it in experiments in my laboratory in Paris. The method is very difficult; the solution is not always good, and as Dr. Taylor has very well said, you must have the exact solution. That has been demonstrated by The Rockefeller Institute in New York, to which we certainly owe a great debt.

For disinfection of a wound of an extremity or of the pleura the procedure is the same. We have three methods. One is by "absorbing" the microbe, one is by killing the microbe by an antiseptic, one is by vaccination. We believe that the growth of infections — surgical infections — can be stopped by changing the composition of the serum of the blood. For this we have two methods. First,

vaccination. For a special microbe we have the autogenous vaccination. But we have another alternative. If you change the composition of the serum of the blood by a chemical substance or a protein substance you can secure very good results and can see the infection decreasing. I am certain that this is so for an abscess of the breast, for some forms of pleuritis, for some diseases of the fatty tissues, for some diseases and infections of the bones. You know that the microbes are living in the blood and in the tissue, because around the microbes is a space where they are not touched by any substance, and when you inject a vaccine or protein substance there you give the blood the power to overcome the microbe. When the microbe is touched by the blood or plasma it is killed.

Dakin's solution is a very good disinfectant for washing the wound and taking off all the bad cells. We were certainly very grateful to the Rockefeller Foundation in Paris during the war for its assistance in supplying it. In the beginning Drs. Carrel and Dakin were working under very great difficulties; they could not do all the experiments that they wanted to do. We lost at least seven months and more than ten thousand men by this handicap.

DEMONSTRATION

Dr. Taylor here showed the materials used in making up the apparatus required for the use of Dakin's solution. He called attention to the importance of observing the minutiæ of the technique as taught by Carrel. A number of infected wounds being treated by the Carrel method were shown and a large granulating wound, treated by Dakin's solution, was grafted by Dr. Char. The front of the thigh was anesthetized by injecting a 0.5 per cent solution of novocaine into the region of the femoral and lateral cutaneous nerves of the thigh just below Poupart's ligament. The grafts were small pinch grafts raised with the point of a fine straight needle, and cut with a sharp scalpel. The wound after being dressed was covered with a piece of paraffined gauze, over which a gauze compress moistened with saline solution was placed.

DISCUSSION

Dr. Tuffier called attention to the necessity for frequent bacterial counts. He said that a platinum loop on a glass handle is used to secure smears from all parts of the wound. Bacterial counts are made frequently, and graphic charts of the counts are kept for each patient.

Question: Do you use Dakin's solution for an overgrowth of granulation tissue?

Dr. Taylor: In our experience there is little tendency toward the overgrowth of granulation tissue when Dakin's solution is used in a wound. Here the granulations are firm, pink, and close together. They make an excellent base for skin grafting after Reverdin's method. In very dirty, necrotic ulcers the curette is frequently used in preliminary treatment, or the ulcer is actually excised, or in some cases the base is swabbed with pure carbolic acid followed by tincture of iodine before the Dakin's solution is started.

Question: Is the Dakin's solution used continuously?

Dr. Taylor: No. As a rule the tubes are flushed every two hours. In some cases, when we have flat, open ulcers, compresses soaked in Dakin's solution are

changed by the nurse every two hours. In large empyema cavities, the patient is turned on the sound side and the cavity filled with Dakin's solution, which is allowed to remain in the cavity for about twenty minutes. This is done every two hours. Of course if there is a bronchial fistula, this cannot be done. The procedure spoken of by Dr. Tuffier a few moments ago may be tried.

QUESTION: Have you had any experience in the use of Dakin's solution in tuberculous pleuritis?

DR. TUFFIER: In these cases the general condition of the patient is greatly helped by the use of Dakin's solution, but we seldom have a cure of the tuberculous pleuritis.

DR. TAYLOR: Our experience has been similar. During the past year we have treated several of these cases without a death and with marked improvement. In no case, however, have we had a permanent closure of the fistula.

VISITING SURGEON: During the war we had large numbers of Chinese coolies in our care. Many of these had very extensive tuberculosis of the pleura. We used to fill up the cavity with the solution. Of course they all died. Most Chinese with tuberculous pleurisy do die.

QUESTION: Do you use Dakin's solution in psoas abscess?

DR. TAYLOR: In view of the impossibility of reaching the site of the infection in such cases, we do not use Dakin's solution.

QUESTION: Is the solution stable in sunlight?

DR. TAYLOR: The stability of Dakin's solution depends largely upon the alkalinity. If it gives a definite pink color with an alcoholic solution of phenolphthalein, it will be fairly stable even in white bottles in the ward. Direct sunlight has a moderately deleterious effect upon it. Potassium permanganate is often added to the solution to give it a faint pink color. This is simply to heighten its visibility and has no other effect, good or otherwise. We here insist upon daily estimation of the strength of the solution we are using. Titration takes a moment only. The amount of 0.1 N sodium thiosulphate solution used in the titration is an index of the chlorine strength.

I have here large graphic charts, which we shall be glad to distribute. These charts give at a glance the percentage of sodium hypochlorite (NaOCl) in any solution examined.

OPERATIVE CLINIC

Participants:

Dr. Théodore Tuffier
Dr. Adrian S. Taylor

CASE I. ANKYLOSIS OF HIP. DR. TUFFIER

A male Chinese. Nine months previous to admission he had an acute onset of some inflammatory process in the right hip. The pain and swelling lasted three months and then subsided. Contraction of the thigh then began. On admission the thigh was found flexed to an angle of 120°, adducted, and internally rotated. X-ray examination showed an old posterior dislocation with the head of the femur ankylosed to the ilium and ischium.

Operation. Vertical incision on latero-posterior aspect of thigh, exposing upper third of femur. Wedge-shaped piece through entire thickness of the bone removed below great trochanter with base of wedge latero-posterior. By alternate flexion and extension the thigh was brought down to an angle of 20° with the vertical. Patient to be put in Balkan frame, with traction to perfect the alinement.

Dr. Tuffier made the following observations upon cases of this kind. The old infected area of the joint must be left alone. The base of the wedge removed should be in such a position that the adduction and flexion deformity may be best corrected and the cut bone surface lie in as close contact as possible when the leg is straight. More primary extension at time of operation may be obtained by alternate flexion and extension than by simple extension. Further stretching of the muscles and alinement must be obtained by traction.

CASE 2. ADENOMA OF THYROID. DR. TAYLOR

A female Chinese, aged thirty-two, married, presented herself for relief because of a large growth in the right side of her neck. This growth was first noticed ten years ago, and had slowly and continuously increased in size. No symptoms had been noticed other than those attributable to the mechanical pressure.

Examination showed a typical unilateral adenoma of the thyroid. No evidence of hyperthyroidism could be found. The tumor occupied the right lobe of the gland and was the size of a large orange.

Operation. Attention was called to the following points in the operative procedure: A transverse collar incision was made low down in the neck in a skin fold, and flaps of skin and platysma were reflected. The sterno-hyoid muscle was separated from the underlying sterno-thyroid, and then the latter muscle was dissected away from the gland. Ample exposure was obtained by retraction without division of either muscle.

Tissues were gently pushed back along the lateral aspect of the gland with a Küttner gauze dissector. This manœuvre was used to demonstrate one of the means of protection of the recurrent laryngeal nerve. After this dissection, the lobe of the thyroid containing the adenoma was easily raised from its bed. The vessels at the superior pole were caught and divided between clamps after they had entered the gland substance. Other straight clamps were placed on vessels

along the lateral aspect of the gland, the vessels being caught "intracapsularly." These clamps hanging to the capsule formed a line posterior to which all tissues were reflected. In this way, the danger of injury to the nerve and the parathyroid bodies was minimized. The capsule was incised from above downward, superficial to the line of clamps, and the large adenoma was excised with a moderate amount of normal parenchyma, the line of excision being superficial to the posterior layer of the capsule. As the midline was approached, the vessels in the medial aspect of the capsule were likewise clamped with the edge of the fibrous capsule. Several perforating vessels in the body of the gland required individual ligation. Hemostasis was secured by fine black silk, transfixed in a figure-eight fashion through each vessel or bleeding point. The medial and lateral cut edges of the capsule were brought together with silk over the raw surface superficial to the posterior layer of the capsule. Muscles and fascia were brought together in the midline with fine silk, and the platysma was closed with a few buried interrupted sutures of the same silk, the knots being tied on the under surface of the muscle. The skin was closed with fine silk interrupted. Perfect hemostasis was secured, and drains were not used. Short straight needles, 1.5 cm. in length, were used for the transfixion sutures in the depths of the wound. The special needles, the clamps, and retractors used in this operation were designed by Halsted many years ago, and the operation itself followed the lines laid down by him (1).

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1. Halsted, W. S., The operative story of goitre, Baltimore, 1919.

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

SUMMARY

PARTICIPANTS:

DR. J. PRESTON MAXWELL
DR. JOHN G. CLARK
DR. DAVID E. FORD
SIR WILLIAM J. SMYLY
DR. JEAN I. DOW
DR. ARTHUR W. T. WOO
DR. FRANK F. SIMPSON
DR. PAUL H. STEVENSON

Friday, September 16. Dr. Maxwell read a paper on the interesting cases of the past year, the first year of the newly opened Women's Clinic, illustrating the paper by radiograms, macroscopic and microscopic specimens, and drawings. The special features of the paper were the discussion of antenatal work with special reference to a case of migraine with hemianopsia; cases of toxemia in pregnancy, with special reference to three cases of threatened eclampsia; cases of Cæsarian section, with their indications and details of technique; some gynecological cases, including a case of sarcoma commencing in a uterine fibroid and recurring after a panhysterectomy; an unusual case of fibroid polypus; and certain pathological specimens acquired during the year, some from within and some presented to the College. Discussion followed the reading of the paper.

Saturday, September 17. The Section met in the operating theatre. Dr. Clark operated on a case of vaginal cyst and discussed its origin and treatment. He then proceeded to give the Section a demonstration of the best methods of performing plastic operations on the vagina, illustrating his remarks by means of plasticine.

A case of procidentia was also shown and discussed.

Monday, September 19. Dr. Ford introduced a discussion on the measurements of the Chinese pelvis, summing up our knowledge of it, and giving details of the results which had been so far published on the subject. Discussion followed and a small committee was nominated by the Chairman, who reported later as to a uniform table which might be used for the recording of the measurements. The principal forms of contracted pelvis met with in China were also mentioned.

Sir William J. Smyly then read a paper on "Eclampsia and Eclampsism," which was followed by discussion.

Tuesday, September 20. Dr. Clark gave a lecture on uterine hemorrhage, its causes and treatment, illustrated by diagrams on the blackboard. He dealt especially with the relation of such hemorrhages to the menstrual cycle and also discussed in detail the use of radium in gynecology and its effects in malignant diseases of the uterus.

By the use of plasticine, Dr. Clark demonstrated an operation for sterility, by opening the uterine horn, no sutures being used to unite endometrium to peritoneum.

Discussion followed.

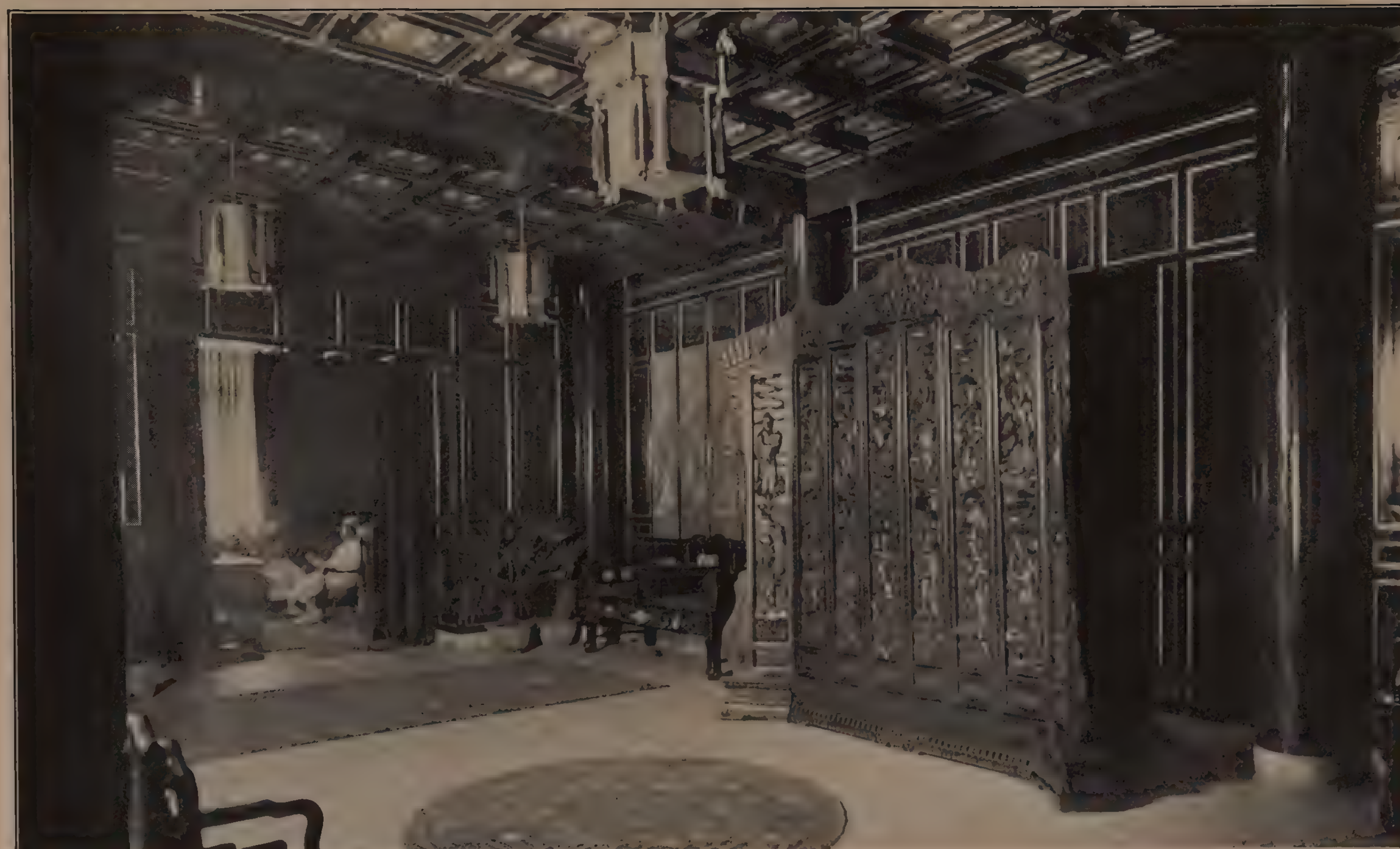
Wednesday, September 21. Dr. Dow read a paper on her maternity work in the famine area, with statistics of 429 deliveries and particulars as to the condition of the patients and means of handling them. Others also spoke on the same subject.

Dr. Woo then demonstrated the use of his modification of Reverdin's needle.

Two cases of chondrodystrophia fœtalis were shown to the Section, and a radiogram of one of these cases.

Thursday, September 22. Dr. Stevenson read a paper on the prevalence and causation of abortions. Discussion followed.

The Section then adjourned to join the Section of Pathology in the consideration of a case of syncytioma presented by Dr. Henry E. Meleney and illustrated by lantern slides. Discussion followed on the diagnosis and treatment of these cases, the case shown being a rare one where death had taken place from sepsis and not from metastasis. There had been, however, hemorrhages on various occasions during the course of the illness, and the invasion of the uterine wall by large syncytial cells was well shown in the sections.



Entrance Hall of the Nurses' Home

Demonstration Room for Classes in Practical Nursing

Graduate and Student Nurses, 1921

Solarium in the Private Patients' Building

INTERESTING CASES OF THE YEAR 1920–21

By

J. Preston Maxwell, M. D.

INTRODUCTION

Before commencing the subject which we are to discuss this morning, let me welcome you all to the meetings of this Section. The Department under whose auspices these sectional meetings are held, owes much already to the kindness of those who are working in China, and I would again invite your hearty co-operation in sending to us specimens of pathological interest, especially tumors, fetuses, monstrosities, and the like. We are prepared to examine any pathological material sent to us, giving the sender a diagnosis at as early a date as practicable, but we would beg that the essential clinical data of the cases be sent to us at the same time as the material. As you perhaps know, several years ago it was found necessary to suspend the women's work, both out-patient and in-patient, at the Union Medical College; and in view of the difficulty of restarting a work of this kind in China I thought that a review of the interesting cases of the first year's work might appeal to you. Some of the cases quoted may seem to you to be commonplace, but it is not the rare cases only which are interesting and instructive. A modern obstetrical department is not complete without its antenatal side, and so we begin with the consideration of several cases which raise problems of importance to us all.

PROBLEMS OF PREGNANCY

No case of serious vomiting of pregnancy has been encountered during the year, but quite a number of cases have been under treatment for the subacute form. Corpus luteum extract has been given these patients in doses of 2 grains, three times a day, and has proved very satisfactory both in primiparæ and multiparæ. In dealing with a symptom of this kind which undoubtedly has its psychological aspect, it is difficult to estimate the value of a drug, but several patients, after using it for a few days, have begged for a further supply, and were emphatic as to the relief it gave them. In one case the corpus luteum in pill form led to acute and immediate vomiting, but in this case the same drug given by injection proved very efficacious. This patient's first pregnancy had ended in a hydatidiform mole, accompanied by pernicious vomiting for several weeks; but the second pregnancy is now well on its way without any untoward symptoms having presented themselves.

Two cases of intense salivation were not relieved to any marked extent, but improved of themselves as the pregnancy went on.

Three cases of definite pregnancy toxemia have been under treatment by the Department. The first of these, a secundipara in the thirties, developed eclampsia in her first pregnancy and had a Cæsarian section performed three weeks before time. In this pregnancy she developed albumen and acetone in the urine at the seventh month. Saline injections by the bowel, sodium bicarbonate by the mouth, and abstinence from all meat, fish, and eggs cleared the urine, and she was con-

fined without any untoward occurrence a fortnight after her proper date of delivery. There was no sign of the Cæsarian scar to be felt, but special care was taken to avoid overaction of the uterus, and the patient was delivered by forceps.

The second case was a primipara, aged twenty-four, who developed a small amount of albumen in the urine a few days before labor. There was also a slight degree of edema of the ankles and legs, with a measure of restlessness which was abnormal. Labor was precipitated by a dose of castor oil and quinine, and the albumen cleared up satisfactorily, though she gave us trouble with mastitis, increased by inverted nipples.

The third case was a secundipara who some hours after her first child was delivered, had an eclamptic convulsion, was comatose for forty-eight hours, and extremely ill. During the early months of this pregnancy she suffered much from headache which was relieved by abstinence from meat and fish. During the last month she developed much edema, a small amount of albumen, and an occasional cast, and the headaches began to reappear. As matters were not improving, labor was induced by bougies about a fortnight before time and she did excellently.

Two other curious accompaniments of pregnancy were encountered during the year. The first of these was in a case under the care of Dr. Douglas Gray. The patient was a secundipara, and towards the latter part of her first pregnancy she had developed an intense gastrodynia, which cleared up as soon as the child was delivered. In the present pregnancy this symptom had reappeared at about the sixth month and the attacks of pain were most severe, irregular in appearance, caused by any article of food or drink, or sometimes coming on independently, and the worst attacks were relieved only by morphia or opiates. There was no sign of any organic disease either of stomach, gall bladder, or kidneys. Towards the end of pregnancy these attacks of pain improved very much and Dr. Gray informed me that they entirely ceased after labor.

The second was a patient, aged thirty-two, the wife of a doctor, who referred her to the Department because of certain abnormalities which had occurred during the pregnancy. She had been married seven years, had one healthy living child, and there had been one miscarriage. In 1909 she had an attack of hemianopsia with intense headache but recovered after a day in bed. In 1911 while on a holiday, she had a second attack with headache and some confusion of speech. In 1915 during the first days of pregnancy, she had very severe headache, a little temperature, and the right arm was numb for twenty-four hours. In 1916 she had one attack like that of 1915. In 1917 just before the miscarriage, she had an attack of hemianopsia, confusion of speech, and numbness, mostly in the hand. In November, 1920, she had an attack of diarrhœa and was ten days in bed. After being up two days she had an attack of hemianopsia with nearly total loss of vision, partial loss of power of speech, using wrong words, much distressed in consequence; numbness of hand, arm, and leg, and slightly of the right side of the face; neuralgic pains over the left side of face and hand; recovered after twenty-four hours. In the eighth week, twelfth week, and sixteenth week of this pregnancy she had uterine hemorrhages lasting from three days to a month. In the twenty-third week she had another attack of hemianopsia, numbness of right arm and hand, difficulty in getting the right word, the condition lasting about half an hour.

On examination the child was found lying in breech presentation and the patient's general physical condition was good. Dr. Howard examined the eyes and found a normal fundus with two degrees of myopia and a good deal of myopic astigmatism, and was of the opinion that the eye symptoms were due to migraine. Dr. Woods examined the patient from the neurological side and came to the same conclusion in regard to the nerve symptoms. Attempts at external version failed and so I allowed the case to proceed as a breech. She delivered herself of a living child, breech with extended legs, although there was no sign of this extension in an X-ray photograph taken a few days before labor. Presentation was a right sacro-posterior, the right buttock rotating to the front. Since delivery the end of June, she has had one slight attack without eye symptoms but attended by headache and numbness, the attack supervening as many of the others have done, on fatigue and worry.

OBSTETRICAL WORK

Turning to the actual obstetrical work: Cæsarian section has been performed eight times during the year, six times in this hospital and twice in the Presbyterian Women's Hospital. Of these, one was a case of central placenta prævia; and to anyone who has had the experience of dealing with this complication by the older methods, the relief from the strain of a case where one is certain to lose the child, and possibly the mother; and the satisfaction of a case, where a fine child is obtained, and the mother has an uncomplicated convalescence, make Cæsarian section for this trouble the operation of choice.

The remaining seven were all performed for contracted pelvis, four were for general contraction involving either an early induction with corresponding risk to the child, or Cæsarian section. In one of these four a Cæsarian section had already been performed in America, and this was the second pregnancy. In a second case, the first child had been lost after a difficult forceps delivery in which the head was crushed, — possibly this was a craniotomy. In the third and fourth cases the patients were primiparæ, came into the hands of the Department early in pregnancy, and the operation was definitely planned, and carried out as the measure of choice.

The other three were cases of funnel pelvis. In each instance attempts had been made to deliver with forceps. In one case the condition had been examined by me myself, the upper measurements of the pelvis being over size, and the impossibility of getting a living child through the pelvis was not discovered till the reason for delay was investigated under an anesthetic. The other two were patients who had been some time in labor, and both operations were performed in the Douw Hospital by invitation of Dr. Hinkhouse. One, a primipara, had been examined outside by more than one person, the waters were broken, but fortunately she consented to a Cæsarian, and both mother and child were saved. The other had been seen before labor came on, and had been warned and entreated to consent to a Cæsarian section. Three children had already died during labor or immediately after delivery and this was the fourth. She steadily refused until, after forceps having been tried, it was clear that no delivery could be accomplished without the destruction of the child, and then she consented. The child gasped only a few times. The mother, however, made a good recovery. One feature of the operation

in the last two cases was the way in which the intestines had become distended, coming in front of the uterus when the abdomen was opened, and welling out of the wound, they could not be replaced until after the removal of the child and the turning out of the uterus; in fact in the last case the reduction of the intestines gave considerable trouble during the closing of the abdominal wall. With the exception of the last-mentioned child, all the mothers and children did well.

Sterilization was performed in only one case, that of the patient who already had had a Cæsarian section. In this case the tubes were cut and tied and the ends buried.

One case of uterine contraction ring has come under our care. The patient, a secundipara, went out in a riksha' as labor was coming on and was conscious of jolting. Whether this had anything to do with the malpresentation is doubtful. When first seen the head was riding over the brim, the cervix was three-fourths dilated with a large bag of waters, and there was no presentation to be felt. Dilatation was allowed to proceed and when the membranes broke the os was fully dilated. A foot could then be felt high up, coming through a tight contraction ring. The patient was moved to the hospital and anesthetized. Pains had ceased completely from the time of the breaking of the waters. Probably this was due to the altered polarity of the uterus as the first stage had been easy and the patient was not exhausted. On examination the condition was as follows: There was a tight contraction ring in the lower uterine segment, with an aperture about 4.5 cm. in diameter; through this protruded a foot and ankle, the toes of another foot, the fingers of a hand and a piece of cord, and on passing one's fingers through the ring, a part of the head was also felt; the child was alive. Circumstances made it impossible to perform Cæsarian section, and so the next best procedure was adopted. Manual dilatation of the contraction ring was carried out as fully as possible and a leg brought down. The arms gave a little difficulty and the head still more, and it took about seven minutes to extract the head without tearing the parts. The child was resuscitated after a great deal of effort, but lived only about seven hours. At postmortem the principal feature was marked hemorrhage into and around the adrenals, a not infrequent occurrence in infants who have died in labor, or after they have been resuscitated with difficulty. Apparently the major number of these contraction rings are due to the cause which acted in this case: the fetal parts being prevented from coming down into the pelvis, the waters drain off into the lower uterine segment, and a contraction ring forms behind the bulk of the waters. They are very difficult cases to deal with.

Only one case has given any trouble with postpartum hemorrhage. The patient was a quintipara with tuberculosis of the lungs and kala azar. She was an inpatient in the Presbyterian Hospital when five months pregnant, and at that time I seriously considered doing a rapid hysterectomy. But she was too ill for the operation. She then improved and went home. About the end of the eighth month she went into labor, and at about 3 A. M. was delivered of a living female child, with no excessive bleeding. I was at the hospital operating at about 10 A. M., when suddenly without any apparent cause she began to bleed so profusely that the only thing to do was to take her to the theater and pack the uterus. There was no further bleeding, but she had a stormy convalescence. After leaving the hospital she was better for a time, then the spleen again enlarged, ascites developed, and she died of asthenia.

Several cases of occipito-posterior presentation have been under observation. As is usual, the majority of these finally rectified themselves.

Two of the cases, both primiparæ, call for special notice. In both for the last three months the presentation was persistently occipito-posterior. One of these finally rectified itself, but the child was still-born owing to a malformation which was found out only at autopsy. The left leaf of the diaphragm was absent, and the left lobe of the liver, the cecum, appendix, all the small intestine, spleen, and part of the stomach were on the left side of the chest, the left lung being a mere rudiment. The placenta in this case was very adherent and had to be removed manually, but microscopically it was normal.

In the second case the malpresentation persisted and the cervix dilated badly. When the mother began to show signs of exhaustion, dilatation was completed manually, and rotation of the head attempted. This could be partially accomplished but the shoulders persistently refused to follow, apparently due to the position of the placenta, and finally I did internal version and delivered, the only difficulty being with one of the arms which had become extended. Convalescence was afebrile in both of these cases.

GYNECOLOGICAL CASES

On the gynecological side the following cases may be of interest. Two cases of severe dysmenorrhœa, which was rendering life difficult for the patients, owing to the monthly pain and invaliding, were treated. One had a thorough dilatation performed, and has been practically relieved of her pain. There was also a prolapsed left ovary but this has given no trouble since the dilatation.

The other case had also some retroposition, and had to spend two to three days in bed every month. Thorough dilatation was performed and then the abdomen was opened and a modified Gilliam operation used to bring the uterus into good position. The ovaries were very large and one showed a small follicular cyst. Half of this ovary was removed and both ovaries were drawn well up out of Douglas's pouch by a fine stitch passing through the broad ligament just below the tube. The result has been very satisfactory, menstruation having been regular and practically painless since that time.

Two cases of abdominal tuberculosis have been treated. In the one there was a history of an attack of peritonitis some eight years previously and the patient was sterile. A tuberculous pyosalpinx was found on the right side, and the tube on the left side was sealed. The pyosalpinx on the right was removed and a plastic operation done on the left tube, but the probability is that as far as the sterility is concerned the operation will be unsuccessful.

In the other case the provisional diagnosis before operation was tuberculous pyosalpinx. An appendix operation had previously been performed and the patient's father had died of intestinal tuberculosis. At the operation a large tuberculous mass was found involving the cecum and base of the appendix and adherent to the back of the uterus. This tuberculous mass, consisting partly of bowel and glands, extended down to and involved the tissues of the posterior abdominal wall. It was freed from the uterus, a portion of omentum was interposed, and it was otherwise left alone. The patient made a good recovery, and gained fifteen pounds in weight during the next two months. The pain in the

iliac region, which had been very severe, disappeared after the operation. Of course the prognosis for such a case is not good, for even a resection of the cecum would not overcome the disease. However, a letter just received from this patient, who was sent home to America, states that she is in good health, acting as a librarian, that the mass is smaller and harder, and that the consultant is quite satisfied with her progress.

Several cases of fibroid of the uterus have been treated during the year, among them the following are of interest:

A woman, aged forty-eight, came to the clinic with a tumor up to the umbilicus which was causing dysuria and difficulty in defecation. This urinary trouble had existed a full year and there had been a period of chronic indigestion of which she complained more than of the tumor. It proved to be a large cervical fibroid (Figure 1) and was removed by panhysterectomy. On microscopical examination the tumor in one part was found to be very cellular with many mitoses, and I predicted an early return of the trouble. The patient, however, made a very rapid recovery from the operation, spent the twenty-second day of convalescence at a Presidential reception and the twenty-third day at the Summer Palace. She remained well for about six months and then began suddenly to complain again of dysuria and difficulty with defecation. These difficulties rapidly increased, she was brought to Peking and found to have a large recurrent tumor in the pelvis, reaching well up towards the umbilicus. An exploratory operation was undertaken as obstruction was becoming serious, a large irremovable malignant growth was found, and it was clear that an inguinal colotomy would probably soon be blocked by the spread of the disease. A transversotomy was done and was a great success, relieving the obstruction and giving very little trouble. But a few days later first one leg became blue and swollen, then the other one followed suit. They became about twice normal size, and greatly inconvenienced the patient, who suffered a good deal from pelvic pain for which morphia was freely given. After about a month she sat up on the bed pan one morning, lay back, became unconscious, and died in about fifteen minutes from pulmonary embolism. At the autopsy the clot was found to have been detached from one of the veins in the right groin; the growth which was frankly sarcomatous was invading a piece of the small bowel, and the ureters passed right through it.

In this connection it may be of interest to note that we had one other case of pulmonary embolism. The woman had had a baby six weeks before, and had a slight mastitis but nothing of serious consequence. She went out into the yard and stooped to get some clothes, was seized with pain and difficulty in breathing, got into the house, became unconscious, with very rapid respiration, and died before I could get to her.

A case of a small fibroid of the ovary which was causing much pain and in which the uterus also contained fibroids, was dealt with by panhysterectomy and did well. One very interesting case of fibroid polypus (Figure 2), was seen in consultation at the Presbyterian Women's Hospital and was operated upon there. There was a swelling filling the pelvis in a woman fifty-two years of age, causing some dysuria and difficulty in defecation. The os externum could be felt undilated high up behind and the feel of the mass in front was almost like a pregnancy. At the operation I intended to do a panhysterectomy but finally discovered that I was

Figure 1. Fibroid of cervix undergoing malignant change

Figure 2. Fibroid polypus which expanded anterior cervical wall

dealing with a fibroid polypus which had expanded the cervix, the anterior wall stretching much more than the posterior wall, and the os externum remaining undilated. She did well.

Three cases were explored for sterility. In one tuberculosis of one tube was found with signs of old peritonitis. In another there was retroversion, but in this case the left tube, ovary, and round ligament were completely absent, the right ovary double normal size and burrowing into the broad ligament. A part of this ovary was resected. In the third case a persistent retroversion was corrected by means of a modified Gilliam operation and the uterus thoroughly dilated and curetted.

Two most interesting cases of malformation were seen in consultation at the Presbyterian Women's Hospital. In one there was complete absence of the vagina with a uterus little under normal size and a blood cyst in the right ovary, the tube not being distended and there being no sign of a hematometra.

The other case was that of a girl in a girl's school. Doubts had arisen about her sex and on putting her under an anesthetic the following condition was found. There was a well-marked penis with hypospadias. Beneath the urethral opening there was a small vagina containing a fruit stone. At the end of the vagina was a small lump evidently the rudiment of a uterus. Two glands could be felt near the internal abdominal rings almost certainly testes. The case was one of male pseudohermaphroditism, and the advice was given that the girl should change her sex and become a boy, or rather a young man, for she was seventeen years of age. The breasts were of the male type in this case, the voice husky, and the thyroid cartilage was prominent.

Pathological material from a good many interesting cases has been received by the Department during the past year. Among other specimens a fibroid tumor of the ovary of unusual size and weight was received from Dr. Wylie of Paotingfu. It weighed twenty-seven pounds, was easily removed, and on microscopical section showed no signs of malignancy.

Dr. Ford of Taiyuenfu sent us a portion of a tumor of the cervix and scrapings from the same uterus. The cervical tumor proved to be an adenoma but the endometrial scrapings were typical adeno-carcinoma. One case of our own deserves special mention.

During the year four babies were lost at birth, or shortly after. I have already mentioned the cases of three of them: i. e., one still-born with malformation of the diaphragm, one which died seven hours after a very difficult breech delivery due to a uterine contraction ring, and one in a case of Cæsarian section, attempts having been made to deliver with forceps and the case having been in labor for some time. The fourth was perhaps the most interesting of them all. The mother was an Austrian, a secundipara in the thirties. Her first child was born after a long labor, a 10-pound male child, but healthy, and it is still alive. During this pregnancy the mother who had become very stout, suffered a great deal, with much vomiting and wretchedness, especially from the third to the fifth months. The latter part of the pregnancy was not specially marked by illness, but she was not well. Labor came on to the day and was not specially prolonged or difficult. She delivered herself of an 11½-pound female child, which came out blue but cried fairly well. Breathing was shallow but the lungs seemed to expand all over,

and oxygen and artificial respiration restored it to a fair color, but only for a short time. It became blue and after an hour or two it was clear we were losing ground, the intervals of good color becoming shorter and shorter. Dr. Douglas Gray was called in consultation and suggested bleeding, which was done without relief. The child died after four and one-half hours and a postmortem was obtained. The liver appeared large but was smooth and did not really weigh much over normal. There were no spirochetes to be found on microscopical examination. The spleen was about normal size, there was a small infarct, and it was adherent to the diaphragm. There was a little free fluid in the abdominal cavity. All the organs with the exception of the ovaries appeared normal on microscopical examination, and the foramen ovale and ductus arteriosus showed no abnormality. But the ovaries were hyperplastic to a remarkable degree, many cysts being present, and the ova had nearly disappeared (Figure 3). I shall be very pleased if any of you can throw light on the cause of this trouble.

CONCLUSION

In closing I present two cases for discussion as to the best method of treatment, I am sorry that it is impossible for me to show you the patients themselves, but on one Dr. Clark will operate tomorrow.

The first case is that of a woman, aged twenty-five. She was in good health till she became pregnant. In the last three weeks of pregnancy she began to suffer from toxemia, slight trace of albumen, restlessness, and anemia. The pelvis showed a little general contraction. Nothing abnormal was noticed on examination before labor. The head came down fairly well but there was a certain amount of primary uterine inertia and the labor was terminated by forceps, but as the head came down there appeared a swelling at the vulva about the size of a small hen's egg, which as labor progressed, protruded outside, and had to be very carefully protected, and returned when forceps were applied and the child delivered. She had a long rest in bed owing to trouble with the breasts, but on rising immediately began to suffer from this swelling which appears at the vulva on straining. The uterus is retroposed and there is slight descent. Dr. Clark, who has kindly seen the patient with me, diagnoses the swelling as a vaginal cyst, and will operate on her tomorrow.

The second case is that of a woman of thirty-two. She is a Swiss and of a nervous temperament. She was strong and well till her first confinement, which was badly managed and left her with a huge tear of the perineum, which was not sewed up. She was six weeks in bed. The child born on this occasion is alive and well, aged nine. In October, 1912, she had a second pregnancy. She was in Switzerland, was much worried at the time, had a great deal of vomiting, and abortion was induced at four months. In September, 1913, she was suffering from backache and probably also from prolapse, was in a weak nervous condition, and was persuaded to have a fixation operation performed. Exactly what was done is not known, save that the tubes were cut, a centimeter of each removed, and the ends buried. After the operation she was better till a year later, when the pain in the back recurred and in addition there was constant burning pain in the region of the cervix. This has persisted ever since, she has been treated by local applications and douches many times without any permanent benefit. At present she is a

Figure 3. Uterus and ovaries of new-born fetus. The ovaries show a marked cystic change. $\times 2$

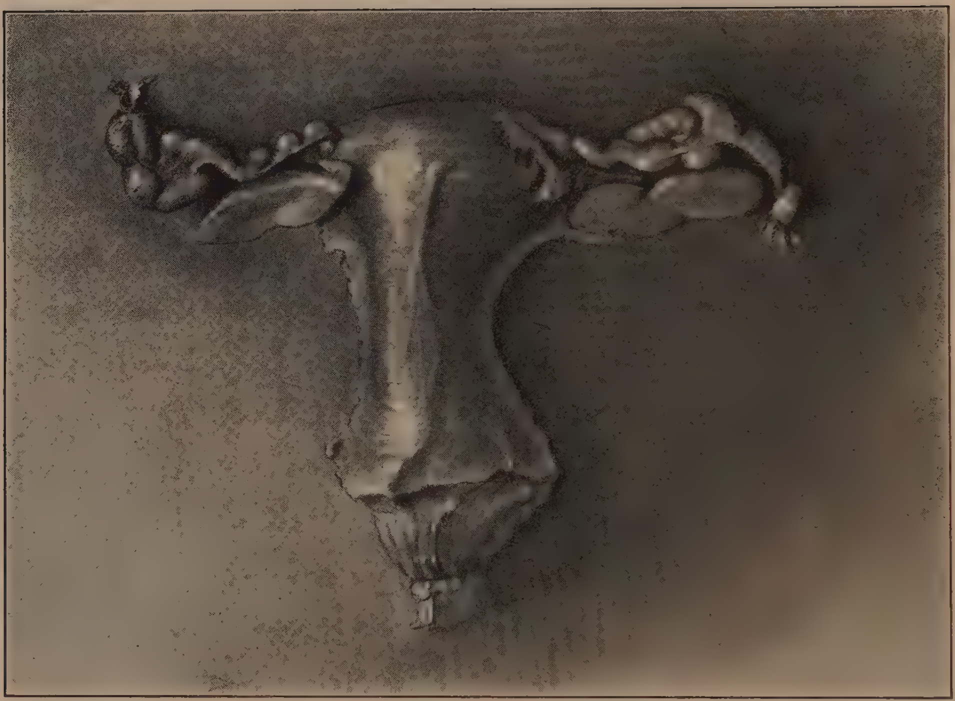


Figure 4. Uterus and ovaries of new-born fetus, normal, for comparison with Figure 3. $\times 2$

neurotic woman, blood and urine normal, and she is in fair physical condition. She feels her inability to have children and deeply regrets having permitted the previous operation. The cervix is cleft to the left, edematous and chronically inflamed. The uterus is bent acutely at the cervico-uterine angle, anteflexed, about normal size, and apparently fixed to the anterior abdominal wall. She is anxious that I should open the abdomen and try to reconstruct the tubes, and probably if this were successful and she had another child she would have much better health. Alternatively the cervix should be removed, but this of course will not relieve the mental attitude. Perhaps the best method would be to remove the cervix, at least the whole vaginal portion, and then explore from above, and be guided by what one found there as to the possibilities of reconstruction, but I have not fully made up my mind on the subject and shall be glad to hear your opinion on the matter.

ECLAMPSIA AND ECLAMPSISM

By

Sir William J. Smyly, M. D.

INTRODUCTION

Eclampsia has been described as the disease of theories, but in the following paper I shall limit myself to what I believe to be well ascertained facts.

Eclampsia is synonymous with convulsions, and puerperal eclampsia applies to convulsions of all kinds occurring in a woman before, during, or after labor. It is an unsatisfactory term because it includes cases which are essentially different, and the same objection applies to toxemia, and to speak of eclampsia without convulsions comes very near a contradiction in terms. We must, therefore, scrap our present nomenclature and discover some name which will include all those cases which are essentially similar, while excluding those which are not.

Schmorl in 1893 published the results of his investigations into the pathological anatomy of puerperal eclampsia, confirmed by Lubarsh in 1895. The conditions described by Schmorl were chiefly characterised by thrombosis of the small blood vessels, necrosis of the cellular elements of the tissues, and hemorrhages. These conditions were found by him in all the autopsies which he made, upon nearly one hundred women who had died from eclampsia, and were present in the kidneys, liver, brain, heart, lungs, and indeed in every part of the body; and, as they were not found to the same extent in any other disease, he felt himself justified in concluding that here was a disease peculiar to lying-in women, and their new born children, and characterised by certain definite anatomical conditions which were considered by him to be essential to and characteristic of the disease. Therefore, when these conditions were present, the case was one of eclampsia; when they were absent, it was not. The blood in eclamptic women is thicker than normal, of higher specific gravity, and contains, as Kollmann discovered in 1897, an abnormal amount of fibrin and, as Schmorl pointed out, a special tendency to coagulate in the blood vessels. The anatomical changes found throughout the body after death, by him and by Lubarsh, appear to have been caused chiefly by this coagulation in the small vessels, and the consequent necrosis of and hemorrhages into the tissues supplied by them. In a subsequent paper he described the postmortem examination of some cases which had died in coma without any convulsions, in which the same pathological conditions were found; therefore they were cases of eclampsia, though without convulsions.

It has been known for a long time that, as a rule, convulsions are preceded by a complex of symptoms which we have been accustomed to call the pre-eclamptic state. Most of these cases, however, do not have convulsions, but whether they do or not, the disease is evidently the same. It has already been stated that one of the essential characteristics of this disease is hemorrhage, most commonly minute petechial hemorrhages, but occasionally very extensive, serious, and even fatal in amount. Anyone who has had much experience with eclampsia must have met with such cases, where the bleeding occurred into the brain, into the eye,

into the peritoneal cavity, or under the skin; but it is only recently that our attention has been called to the fact that intra-uterine hemorrhage also may be caused in the same way. Since then all these conditions, namely, pre-eclamptic toxemia, eclampsia, eclampsia without convulsions, and accidental hemorrhage are generally symptomatic of one and the same disease, it is desirable that they should be grouped under one name, and I think the suggestion made by Dr. Bar of Paris an excellent one that, while retaining the term eclampsia for those cases in which there are convulsions, we should employ the word eclampsism for those in which there are none.

TREATMENT OF ECLAMPSISM

In the treatment of eclampsism obstetricians have been influenced chiefly by their views as to whether its causation is ovular or maternal. Those who consider that the disease is due to the ovum maintain that its removal, at the earliest possible moment, is the only rational procedure; while those who look upon the disease as the result of faulty metabolism on the part of the mother, direct their efforts towards combating her toxemic condition. The extreme members of the former group resort to Cæsarian section in every case after a single convulsion; the extremists of the other group leave the delivery altogether to nature. Neither of these methods has fulfilled the expectations of its advocates. I think there can be no doubt that both the ovum and the mother participate in the production of the eclamptic condition, the fact that it occurs only in connection with pregnancy being sufficient proof of the former, and the good results obtained by limiting the mother's food the latter. We know that in digestion a very important part is played by the blood, that this digestive power is far in excess of normal requirements; but that this power is not unlimited we learn by experience when we eat too much and do too little. During pregnancy the maternal blood has the added task of dealing with material poured into it from the ovum, and the occurrence or not of toxemic symptoms depends upon whether it is equal to that task. Some years ago Doctor Tweedy, when master of the Rotunda, formulated a system of treatment which obstetricians in Dublin and in other places have since adopted with remarkable success, the most important feature of which is the restriction of the diet of the patient to water, or in other words starvation. A remarkable confirmation of the advantages of this method of treatment has been furnished by what has occurred in Germany during the late war where, consequent upon the lack of food there, due to the blockade, the proportion of cases of eclampsia to the births sank, according to Warnekros and Schülein, to one half, and was estimated by Ruge at one third the normal pre-war rate; and further that the cases were of a milder type, as shown by the reduction of the death-rate from 20 per cent to 8 per cent.

In describing the treatment of eclampsism in the Rotunda Hospital I shall do so under three divisions:

1. Treatment of pre-eclamptic toxemia.
2. Treatment of eclampsia.
3. Treatment of accidental hemorrhage.

In pre-eclamptic toxemia treatment should commence at the earliest moment possible, hence the importance of prenatal clinics. The patient should be put to

bed and given water only, with some laxative medicine. If improvement follows, some light food, such as milk, may be given, noting carefully the result; if she continues to improve she may have more food, but if a relapse follows any addition, then labor must be induced. The benefits to eclamptics which have been claimed for a milk diet are only comparative. It is only better than other foods.

When a patient first comes under treatment after one or more convulsions she is given 0.5 grain morphia hypodermically. Her stomach and rectum are thoroughly washed out by means of a stomach tube until the fluid returns quite colorless, requiring as a rule several gallons of water; about half an ounce of Epsom salts is passed into the stomach through the tube before it is withdrawn. If the patient is conscious, she is encouraged to drink as much water, to which bicarbonate of soda is added, as she will take. If unconscious it is infused into her cellular tissue, under the breasts or elsewhere. As regards complications, precautions must of course be taken to prevent the patient from biting her tongue, or otherwise injuring herself. But a common cause of death, and one easily prevented, arises from allowing an unconscious patient to lie upon her back. In such cases an enormous amount of mucus is likely to collect in the nasopharynx, and in that position will be drawn into the lungs, drowning her in her own secretion, or causing a septic pneumonia which subsequently proves fatal. It is, therefore, of very great importance that these patients should be kept in a semiprone position; and should any symptom of impeded respiration occur, her head should be drawn over the side of the bed, well down to the floor, when usually a large quantity of mucus pours out of the mouth and nostrils and respiration is restored. We never sweat our patients now, as we believe that it does more harm than good. Chlorides in any form are injurious, and therefore we employ the bicarbonate instead of the chloride of sodium for infusions, and chloroform is employed under exceptional circumstances only.

As regards the delivery of the patient, it is completed as quickly as the special circumstances of each case will permit, without increasing the risk to the patient. Accouchement by force, by which I understand version and extraction through an undilated cervix, does not fulfill these conditions, because it materially increases the danger to the mother, and should be abandoned.

The treatment of concealed accidental hemorrhage by abdominal section and hysterectomy, was originated with Dr. William Bagot, now of Denver, Colorado, when he was my assistant in the Rotunda Hospital, and was successfully carried out by him upon a patient in the Extern Maternity. But it was several years before any other operator ventured to follow his example; and when in 1910, Dr. Amand Routh published a report upon 1,280 cases of Cæsarian section collected from obstetricians living in Great Britain and Ireland, only three had been performed on account of accidental hemorrhage. Since then, however, it has been resorted to more frequently, and is now, I believe, generally recognized as advisable, at least in those cases in which the patient is not in labor and the hemorrhage is concealed. Since the introduction of this line of treatment, which in my opinion marks a distinct epoch in obstetric history, we have learned that the actual conditions are very different from what we had imagined them to be. We knew, of course, that the placenta was detached, and that the uterus was distended with blood, and assumed that, because this effused blood was not expelled, there must have been a weakening or paralysis of its walls, but its true cause had not been deter-

mined. Now we know that the blood is poured, not into the uterine cavity alone, but also into its muscular wall, which is suffused with blood, separating and no doubt injuring its muscle cells. This accounts sufficiently, not only for the yielding of the walls to the pressure of the blood, but also for the extreme difficulty which has sometimes been experienced in controlling postpartum hemorrhage. In many of the reported cases there was hemorrhage also into the pelvic cellular tissue, especially between the folds of the broad ligaments, and into the peritoneal cavity. In two cases, reported by Whitridge Williams in 1915, in which the uterus had to be removed, the microscopic examination showed that the hemorrhage had spread apart the individual muscle fibers and bands, and in places was associated with considerable edema, and that it apparently was not connected with the larger vessels. Section through the placental site showed similar changes in the muscular wall; but the deciduæ were normal, except for small hemorrhagic areas. In this region many of the larger veins were almost completely filled with large thrombi. The large arteries were normal, but many of the smaller ones presented changes in the intima, and in many places defects were observable in it. The principal pathological changes presented, therefore, were thrombosis of the veins, necrosis of the intima of the small arteries, and hemorrhages into, and edema of the uterine walls. This remarkable condition of the uterus has, during the past few years, been frequently noted by other observers, in connection with accidental hemorrhage, and at a single meeting of the Obstetrical Section of the Royal Society of Medicine in London, in November, 1916, no fewer than eight cases were reported. This condition has been described by Couvelaire as uteroplacental apoplexy, and although he considers it to be a constant feature in accidental hemorrhage, yet he regarded it as merely the result of overdistention of the uterus. That in my opinion is a most important question, because if the effusion of blood into the muscular tissue were merely the result of overdistension, then its connection with eclampsia is not so obvious as I suppose it to be. But if, on the other hand, it can be proved that this condition is not caused by overdistension, that it occurs only in patients with symptoms of toxemia, and that the anatomical conditions associated with it closely resemble those which cause hemorrhages in other parts of the body in eclampsia, then it would seem to me a justifiable conclusion that it is due to the same cause. As regards the theory that the remarkable condition of the uterus is merely the result of its overdistension, I may refer to some experiments carried out by Dr. Arthur H. Morse in Yale University Medical School (1). He was prompted to make those experiments by two cases of concealed accidental hemorrhage, in which he was struck by the resemblance between the conditions there found and those which are met with in cases of ovarian tumors with twisted pedicles. His first endeavor was to discover whether sudden overdistension could, as had been affirmed, produce such phenomena. With that object he exposed, by abdominal section, the uterus of a pregnant bitch, inserted a canula into it, and injected saline solution until it was distended almost to bursting. No ill-effects, excepting abortion, followed; and when the abdomen was again opened, after forty-eight hours, the previously distended horn was found to be entirely normal, without any sign of injury. That experiment showed that even extreme and acute increase in intra-uterine pressure did not cause extravasation of blood into the myometrium. Some time after he made a further series of ex-

periments upon rabbits, with a view to ascertaining what the results of venous obstruction in a pregnant uterus would be. He discovered that, when all the veins returning blood from a pregnant horn had been ligated, it became deeply cyanosed and distended, at first functionating, but ultimately firm, tense, and resistant to pressure. After from two to four hours it was found enlarged to about twice its former size, and was quiescent, muscular action having ceased. When incised, the uterine cavity was found filled with blood, which surrounded the unruptured fetal sacs; the placentæ were partially or completely separated from their attachment and minute extravasations of blood were visible in the myometrium. The microscope showed numerous extravasations in the decidua and into the uterine wall, as well as dissociation of the muscle fibers; in fact in every particular an exact reproduction of the conditions found in cases of accidental hemorrhage.

CASES TREATED AT ROTUNDA HOSPITAL

The following cases, of which I shall give a very brief summary, illustrate very clearly the connection between eclampsism and accidental hemorrhage.

Case 1. This patient was admitted to the Rotunda Hospital in 1915 under Dr. Tweedy's care. She was pregnant about seven months. Her face, legs, and thighs were edematous. She complained of intense headache, dimness of vision, and vomiting, secreted very little urine, which contained numerous tube-casts and became almost solid when boiled. Her blood pressure was very high, — a typical example of the pre-eclamptic state. She was restricted to water and the usual treatment was adopted. She improved for a time but a week later suddenly complained of violent abdominal pain; a bloody discharge, which gradually increased to a considerable hemorrhage, escaped from the vulva; it was apparently controlled by a vaginal plug, but her general condition grew steadily worse. The face became blanched and cold, the features pinched, the pulse more rapid and weaker. The diagnosis was internal hemorrhage. On opening the abdomen a considerable quantity of free blood was found in its cavity, the source of which was discovered in the right broad ligament, and was controlled by a ligature thrown around the ovarian vessels on that side. The uterus also contained a large quantity of blood, the placenta was completely detached, and the fetus dead. The operation was completed without removing the uterus which contracted well. There was no postpartum hemorrhage, and she made a good recovery.

Case 2. I was asked to see this woman in November of the same year (1915) by her family physician who had diagnosed the case ten days before as one of toxemia, and had restricted her to a milk diet, but no improvement had resulted. When I saw her there was anasarca, with puffy face, and swollen eyelids; the urine was scanty and contained a large quantity of albumen. I stopped the milk and gave nothing but water, under which treatment she improved so much that at the end of a week she could take milk; and I discontinued my visits. Ten days later, however, she was seized with violent abdominal pain and fainted. On my arrival I found her in a critical condition with all the symptoms of severe internal hemorrhage; the uterus was firm and hard, and no fetal parts could be felt. Fortunately labor came on immediately and after a few pains a dead infant, the placenta, and a large quantity of blood and clots, were all expelled together. She was very collapsed for a time but made a good recovery.

Case 3. This patient was admitted to the Rotunda Hospital under my care in September, 1917. Her two previous pregnancies had terminated normally at full time. On this occasion she had noticed nothing abnormal until the evening previous to her admission when she was seized with violent abdominal pain and a feeling of distension, and she noticed an increase in the size of her abdomen. When admitted to the hospital she was in a collapsed condition, blanched, cold, temperature 95.4° F., pulse hardly to be felt. Uterus very hard and tender, no fetal parts could be felt. There was no external hemorrhage, urine scanty, loaded with albumen casts in large numbers and some blood-cells. When the abdomen was opened the uterus presented a remarkable appearance; it was dark, almost blue in color, with blood extravasations in patches over its surface, the peritoneal covering being in places raised in large blebs filled with blood, one of which upon the posterior surface had burst, the rent being about an inch long, and there was free blood in the peritoneal cavity. When cut through, the uterine wall showed blood extravasations throughout, the cavity was filled with blood, the placenta completely detached, and the child, of course, dead. After the uterus had been emptied and the wound closed, it contracted well with pituitrin, and therefore I did not remove it.

Case 4. A woman, aged thirty-nine, nonipara; thirty-six weeks pregnant. Was admitted to the Rotunda Hospital on December 7, 1917.

Twelve years previously, her first pregnancy terminated prematurely at the eighth month, in consequence of eclampsia, preceded by headaches and disordered vision, and ever since, the sight in her left eye had been impaired; she was unconscious for a week and the child was still-born. The four succeeding pregnancies were normal, the children living. But after the birth of the last, four and a half years previously, she did not make a satisfactory convalescence; had three abortions subsequently, and was curetted in 1916.

On admission she said she had been ill for about three weeks, suffering from headaches and impaired vision. There was a large ecchymosis on the left buttock. The urine was scanty, and of a bright red color, and contained a large quantity of blood and tube-casts. The child could be easily palpated, presenting the head in the first position. The diagnosis was pre-eclamptic toxemia, and she was treated in the routine manner, introduced by Dr. Tweedy, getting nothing by the mouth but sodium bicarbonate and water. She got little sleep in spite of a hypodermic injection of morphine, and the total quantity of urine passed in the first twenty-four hours was 20 ounces. The blood-pressure was 260 mm. The following day there was no improvement, and some twitching in the muscles of her arms. She was given 0.5 grain of morphine hypodermically. During the following days there was no marked change in her condition; but on the sixth day she seemed to be rather better, and had passed 31 ounces of urine during the previous twenty-four hours, but in quality it was the same as upon admission, and the blood-pressure was still 250 mm.

Considering that she had been restricted to soda and water for five days, since her admission to the hospital, and that she said that she had eaten nothing for two days before then, I thought it advisable to give her some nourishment. Accordingly, at 12.30 P. M. she took four ounces of milk with an equal quantity of barley-water. At ten minutes past one she complained of a violent pain in her

abdomen, and said that she could see nothing. She looked pale and collapsed; her skin felt cold, clammy, and bathed in perspiration; her temperature was below normal, and there was a little reddish discharge from the vulva. Her abdomen was evidently larger, the uterus swollen, hard, and tender, and the fetus was no longer palpable. Her condition, indeed, appeared desperate, but being persuaded that her life could be saved in no other way, I determined to operate immediately. The abdomen having been opened, the uterus presented the same remarkable appearance which I have already described, being much distended, of a dark, bluish purple color, with numerous patches of ecchymosis on its surface. The wall when cut through showed blood extravasated throughout its substance. The placenta was completely detached, the cavity full of blood and clots, and the fetus dead. To save time, which was of vital importance, I closed the uterine incision with a running suture of Van Horn's catgut, otherwise the operation was carried out in the usual manner. Towards its close the patient appeared to be dead, but gradually revived, and was removed to bed. She made a good recovery, though, owing to her toxemic condition, she was still restricted to soda and water for the three succeeding days. Her urine improved rapidly both in quantity and quality, so that on the fourth day it was normal in color and free from albumen.

I believe that a consideration of these cases, together with others published by other obstetricians, is sufficient to prove that many, if not most of the cases of severe accidental hemorrhage are due to conditions closely allied to, if not identical with eclampsism. Although in all the cases, one operated upon by Dr. Tweedy, and two by myself, the uterus was not removed, yet from a consideration of the cases published by others, I have no doubt that in some the uterus will not contract, and its removal is necessary to save life.

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MATERNITY FAMINE RELIEF

By

Jean I. Dow, M. D.

INTRODUCTION

In normal times midwifery has occupied a small place on the program of the Women's Hospital at Changteh. One feels ashamed to make this confession, for it would be a platitude to say that a hospital conducted by women could find no finer scope and could exercise no more useful function, in the physical realm, than by leading the way in the liberation of fellow-women from the meddlesome though well-meant atrocities of the self-taught midwife of Inland China. The city in a suburb of which we are situated is conservative, and on the other hand the limitation of a one-doctor staff during a period of fifteen years discouraged the uncertainties of out-practice so that our record of only a few obstetric cases each year has brought us little fame in the eyes of the Chinese community. But one cannot conduct a general clinic for women and children without receiving convincing demonstration of the urgent call for preventive gynecology, not to speak of saving life and preventing cruelty.

When other forces were lining up last autumn to face the task of life-saving, while we were faced with vanishing clinics and sparsely occupied wards, we began to cast about with anxiety for a fitting part to play, a place from which we might reach not those within the radius of church connection who could be helped by other routes, or those who by proximity to a distributing center might gain notice through personal appeal, but some of those on the outer rim too far away to be anybody but one of the crowd. Then some unknown person also in search of possible avenues of relief, conceived the thought of an allowance for the nursing mother. The press mentioned it, and the solution of our problem came into focus: a free maternity service with a subsequent monthly allowance for mother and child to the end of the famine period.

PLAN FOR RELIEF

The plan was approved by the local committee, the maximum grant fixed at $2.50 per month, conditional upon presentation before the inspector of both mother and child wearing their identification mark, the inspector to be made responsible for the bona fide character of the applicant's claim. For purposes of general investigation and distribution the local Christian Chinese Foreign Famine Relief Society had already put into operation a card system for use through investigators selected from the elders, deacons, evangelists, or church members in the various areas. These men performed the same service for us. Proclamations were issued announcing the terms of the offer and the name and address of the inspector in each locality to whom application should be made. Tickets bore the hospital seal and were made out in sets of three. The applicant received one — her admission slip — on which the inspector filled in number, name, age, residence, family head, occupation, and guarantor. On the opposite face were columns for recording month by month the amounts actually paid. The inspector filed a larger

ticket giving the same facts with additional columns for data to be transcribed from the hospital copy, such as dates of admission, confinement, discharge, sex of child, and amount of grant. The hospital copy recorded, in addition, notes on special circumstances of the patient.

Misappropriation by the family was guarded against by the regulation that unless the child was presented for inspection the allowance would be withdrawn. In actual practice, however, it was found that where the death of the child was reported, the family frequently was in sore straits. Help was continued, therefore, at a minimum rate of $1.00 per month, and where a motherless infant was adopted, the full amount was given. If the mother engaged in a self-supporting family as wet-nurse, her name was deleted from the pay-list. In some instances there were blind or dependent parents, in others sick husbands, and in most others little children. In view of the following notes from the records, one feels little surprise that out of a total of 489 births under the scheme, twenty-five babies and five mothers succumbed at home.

No. 192. Husband, two children, and self fled to Shansi. Sold their quilts to raise money to come home. Have sold even the wheel-barrow (the sole equipment of the bread winner). Mother-in-law ill, unable to rise for want of food.

No. 222. Widow with three children. Family left home. Husband for a time found occasional work in the South Suburb. Finally lived in Beggar's Refuge. Little girl died there. Husband died there ten days ago. Two boys in ragged clothes, one looks ill. Child born on the road, east of Mission Compound gate.

No. 150. Mother and baby normal when discharged. Six weeks later appeared in outclinic, baby emaciated, mother unable to walk without assistance. Boy of five, characteristic famine appearance. Husband's brother appropriated part of the wife's grant to pay debt. Husband had been ill and took part for travelling expenses. Woman and baby readmitted, child of five fed from hospital kitchen. Baby died. Mother redischarged after a fortnight. Full allowance continued. Money again confiscated to pay debts. Mother died of insufficient nourishment.

FINANCES AND SUPPLIES

Anxiety regarding finances was removed at the outset by an immediate appropriation of $4,500 from the Chinese Foreign Famine Relief Society of Shanghai, a further $1,000 following later, with the addition of $700 from other sources, and the question of equipment was greatly simplified by the timely grant from the American Red Cross of goods which had just been opened up. These were rolls of flannelette and flannelette blanketing, thousands of yards of gauze, three cases of large pads, besides layettes, babies' blankets, adhesive plaster, and many other nursery requisites, which, inasmuch as we had not sent in a requisition, created a comfortable sense of the presence of a Co-operator behind the scenes who had planned in advance.

When the day of discharge of the first cases arrived, it was found that families had made, and could make, no provision for even the irreducible minimum of clothing for the new members. It was unthinkable with one fell stroke to cut off a baby of seven or eight days from comfort and warmth and turn it adrift. Material was therefore given to each waiting mother with a promise that the completed garments would be hers against going home day. And presently the Shanghai

Women's Famine Relief Committee, as well as interested Chinese and foreign friends in Manchuria and Hangchow came grandly to the rescue with plenty of padded clothing and comforters, so that every child had a going away suit, cap, and comforter, while hundreds of suits too large for small babies were passed on for distribution to older children. Mothers with thin or ragged garments were fitted out and comforters were given to those in distress.

HELP TO WAITING CASES

In order to check too early arrival, no provision for food was promised during the antepartum period. Hostel space and facilities for cooking were provided. When spring opened, patients were permitted as a special privilege to help themselves to alfalfa shoots from the mission grounds as a substitute for vegetables at prohibitive prices. Some earned their food by sewing, and always a certain number helped in the laundry, partly as a means of subsistence and partly for exercise. Numbers went regularly to the public food kitchen in the East Suburb. Exceptions of course were made from the first, for instance, a blind woman whose husband was a non-provider, was fed for over two months. One of the first cases, whose son had been sold for $5.00, proceeds already spent, and whose sister-in-law had starved, leaving an infant of a few days to be buried alive in the mother's grave, was sent to us to save her from a similar fate. This woman was so emaciated that she was put to bed for a few days and was then supplied with food for over two months.

During the earlier months the nutrition of the babies at birth was so good that we wondered if homes were suffering as great privation as had been supposed, but in the later months when a large proportion of the pregnant period had been passed under unfavorable conditions, it became obvious that infants were being born with a handicap so serious that the object of the scheme might after all be defeated. It was then decided that a sufficient daily portion of grain or flour be allotted to every patient in the antepartum hostel. On the whole we were probably overcareful not to overhelp, as a considerable number were admitted and examined, who never passed through the delivery room, presumably concluding that they would take a chance at home.

SOCIAL CLASS AND HOME CIRCUMSTANCES

The social class and home circumstances of patients are shown in the following summary:

Husbands

	per cent
Laborers without land, including scavengers	52.4
Small land owners; amount 1 to 20 mows (1 mow = $\frac{1}{3}$ acre)	22.2
Small business men; selling peanuts, brooms, cakes	10.89
Non-providers; e.g., opium users, gamblers, beggars, persons mentally deficient, blind, dumb	6.0
Artisans	4.9
Professional; three teachers, one medicine man	0.94
Soldiers; three recently enlisted	0.70
Dead; one shot, one ill, three starved, one cholera	1.89

Sample Cases

Landowner. Six in family — husband, four children, and self. One mow land, irrigated, not sufficient for a family of six, at present prices. Non-Christian.

Artisan (Harness-Maker). Six in family — mother- and father-in-law, husband, and two children. Husband, no work, gone to Shansi. Word received that the grandmother of ninety-four years had been shot dead, one boy shot but not fatally, mother-in-law shot in the arm. House burned.

Laborer's wife told this story. There were two brothers in the family. They lived in a small house, partitioned by a wall reaching only part way to the ceiling. Every salable article had been sold. On the other side of the partition her sister-in-law had recently been delivered. The only dressings used were rags and earth, and these were never changed. Mother and baby died.

Fate of Children

Information on this subject is confessedly incomplete and incidental. Of 1,691 births reported in the antepartum room, 790 children were still living, a mortality of 53 per cent. Such causes of death as were investigated invariably fell under the head of disease, the most frequent single cause being that which is popularly known in Honan as "Chi feng," and in no case did the mother's manner excite suspicion of wilful neglect.

Typical History

Liu, aged thirty-seven.

Births

1. Difficult labor, mutilated.
2. Died second day.
3. Still-birth (?).
4. Died sixth day (Chi feng).
5. Died, one day's illness, abdominal cramps.
6. Cried, but died shortly.
7. Did not outlive first month.
8. Living.
9. Died at one year. Infectious disease (eruptive fever).

Record of Children Lost to Families

Given away:	Five boys, and two girls sent to mother-in-law's home. Two unclassified.
Sold:	Two boys and four girls. (One boy returned, not wanted because he was deaf.) One unclassified.
Starved:	Two boys and four girls.

Circumstances under Which the Children Were Disposed of

No. 90. Two girls sold for $10.00 and $6.00. Family exceedingly poor, children no clothes. Four adults and four children left. Would have died without the money received for these girls.

No. 123. Gave away two youngest boys for lack of food.

No. 149. Sold eldest son, brought back because he was found to be deaf. Youngest very emaciated. Husband mentally deficient.

No. (Not Recorded). Six children in family. Youngest a boy of two years given away because there was nothing to eat, and he was too young to beg. Grandfather died of starvation while mother was in hospital.

No. 201. Sold one daughter. No home. Husband and four children.

No. 410. Husband wanted to sell girl of two years. Wife not willing. Husband left mother and child to beg, and left home.

No. 582. Sent daughter of eight years to mother-in-law. Sold daughter of five years to child dealer. Would not have sold her if they had had any other means of subsistence. Did not know danger of ultimate destination.

No. 629. Daughter forced on mother-in-law rather than sell.

No. 658. Widow maintaining orphan niece in addition to her own two children, though husband died of starvation.

No. 723. Two nieces included in family.

(The impression left on the mind was that either girls or boys were parted with only as a last resort and that mothers were not informed of the magnitude of the white slave menace.)

PHYSIQUE OF MOTHERS

1. All women had moderately bound feet and wore bandages if they could afford them. With few exceptions the journey was made on foot, even to distances of 30 or 35 miles. It was not to be wondered at that nineteen births occurred on the way, one mother having been reduced to sundering the cord with her teeth. One, more fortunate, arrived safely, but armed for emergency with a pair of scissors.

2. To say that we observed no abnormality of the pelvis and at the same time to admit that the pelvimeter was not used as a routine part of the antepartum examination may be to court criticism. It is safer to say that no case occurred of dystocia from disproportion between pelvic and fetal measurements. Internal, antepartum examination was made as a routine. We were pressed for time, and unless there arose a suspicion of contraction, as existed in one case only, the use of the pelvimeter was dispensed with. In this case the external measurements were slightly below the average but labor presented no difficulty.

3. No case of venereal disease was noted. In our experience the classes that supply most of the material for this clinic are wives of soldiers, railway employees, merchants, and coolies, who are often absent from home. In the above list these classes are conspicuously absent.

4. The nipples were well formed and hardy. No case of cracked nipple occurred and no mastitis.

5. There were no cases of toxemia.

LABOR

Labor was undoubtedly marked by less suffering than is experienced by Western women of the working class. As a rule in multiparæ the second stage was brief, sometimes almost to vanishing point. Perineal tissues offered less resistance than in the average Western patient and rupture of the membranes was followed

rapidly, if not preceded, by presentation at the outlet. Of thirty-two primiparæ the average age was twenty-one. Seventy-two per cent were twenty-two or under, 50 per cent were twenty or under; the two youngest were seventeen, the oldest was thirty-three. Slight perineal laceration occurred in 1 per cent of all cases and in one or two of these it might have been prevented by more liberal use of the anesthetic.

The strength and frequency of the contractions was strikingly influenced by posture. So often did a marked slowing up follow assumption of the horizontal position that it became a habit when the patient was placed on the table to observe the effect before draping so that if expedient she could be raised to a sitting posture.

The value of a bowl of hot food in muscular insufficiency was amply demonstrated.

PRESENTATIONS

Vertex (occipito-anterior)	413
Vertex (occipito-posterior)	4
Face	2
Breech	4
Foot	4
Shoulder	1
Hand	1
Total	429

In occipito-posterior and face presentations delivery was spontaneous. In the majority of the breech and foot cases assistance was given with the after-coming head by the "jaw and shoulder traction" method, while resuscitation of the child when necessary was effected by alternate immersion in hot and cold water.

In the shoulder and hand cases internal padolic version was performed.

There were two cases of multiple pregnancy in the series but one pair was born before the mother could leave home. In our case one child presented by the occiput, the other by the breech.

There were two still-births, one due to prolapse of the cord; the other, cause unknown.

Adherent placenta, of which there were four cases, and retained membranes were removed without known exception, normal convalescence following.

Postpartum relaxation yielded to massage and pituitrin or ernutin.

PUERPERIUM

The Mother. Two deaths occurred from sepsis. Whether the source of infection lay in faulty technique or in internal manipulation by the patient herself during the first stage of labor we have no means of knowing. One woman confessed to having palpated the descending occiput and it is a fact that self-manipulation for purposes of investigation is not uncommon, but for the result in these two fatal cases we are safer to carry the odium ourselves.

Procidentia was observed in one whose child was about to be thrown away when the hospital's offer of help reached her. Walked in 10 miles.

The Child. In all, seven babies died during the puerperium, including four very small at birth, one premature, and one having a widely separated cleft palate. (Cause of premature labor, a blow from a man who observed her stealing his vegetables.) We had not the staff nor equipment nor space to set aside for a large nursery and in any case separation from the mother would almost certainly have created undesirable suspicion regarding identity and treatment. But the system cost us two babies accidentally smothered.

One hundred and forty-eight returned for vaccination.

RELAPSING FEVER

Four cases were met within the maternity cervix:

Case 1. Refugee to Chengchow by train. On return trip birth took place at Changte Railway Station. Temperature on admission 104.4° F. Blood examination positive.

Case 2. Child born on main street, Changteh City, near an official home. Mother given 120 coppers and a bowl of flour and sent in 'riksha to the hospital. Temperature on admission 103.6° F. Person swarming with lice. Clothed in filthy rags which were carried out on the end of a pole and burned. Patient was bathed and kerosened. Blood examination showed overwhelming numbers of spirochetes.

Case 3. Had been living in Beggar's Refuge. Developed attack in convalescent ward. Clothes burned (?) or disinfected. Blood examination positive.

Case 4. Had been in waiting ward eleven days under no restrictions as to going out. Did not complain until the onset of labor when temperature was 103° F. Her stool was examined and ova of *Ascaris lumbricoides* found. Passed two *Ascaris* worms and temperature fell to normal. Blood examination omitted by default. On ninth day temperature began to rise. Blood examination showed the *Spirillum.*

Of the modification of salvarsan sold by Allen and Hanburys, Limited, we used 0.3 dose and found that thirty to thirty-four hours elapsed before the temperature returned to normal, while in children of ten years or less a dose of 0.15 produced the effect in half the time. Of all adults treated two or three showed a secondary rise seven or eight days later not exceeding 100.5° F., which subsided spontaneously in a day or so.

In concluding I venture to hope that in the discussion this morning some light may be shed on the problem not only of training midwives, but of inspiring those who are trained with the ambition, for love of humanity, to serve their fellows in regions far afield.

SOME PRACTICAL ASPECTS OF EMBRYOLOGICAL RESEARCH IN CHINA

By

Paul H. Stevenson, M. D.

INTRODUCTION

One of the fine inspirations that has come to the laboratory workers of this institution from the week that is just drawing to its close is to be found in the genuine interest manifested by so many of the visitors in the various research activities upon which these workers are engaged. The readiness, in most cases the eagerness, with which the vast majority of medical missionaries in China are willing to put to practical test and actual use every advance in the knowledge of medical conditions in China that this or any other institution is able to place at their disposal constitutes a very real stimulus to those whose days are spent among test-tubes and microtomes. Although this interest is particularly manifested with respect to progress in the diagnosis and treatment of the diseases that are peculiar to China and with which many have had little or no opportunity of coming into contact before taking up their present work in China, yet the same expectancy and willingness to profit by our studies along more generally scientific and less strictly clinical lines (such as physiology, biochemistry, and anatomy) is also evident upon every hand. It will be quite impossible for those of us so employed to return to our work without the feeling that the opportunities and obligations naturally imposed upon us by the inherent spirit of the work that engages us, will be multiplied several times by this added consciousness of the confident expectancy on the part of the large numbers of medical missionaries in actual clinical contact with the great masses of Chinese.

It is with pleasure, therefore, that I am able to report briefly upon the beginning of a particular type of research which is being undertaken in the anatomical laboratories of this institution and which, in addition to its broader interest along the lines of anthropology and racial embryology, is capable of making a specific contribution to the solution of some of the clinical problems of those engaged in obstetrical and gynecological work among Chinese women. Viewed in this light, the work in question represents not so much an effort to collect and preserve a type of material which, though plentiful in China, is very seldom preserved and made available for scientific study, as a start towards the investigation of the causes and conditions which bring about the waste of human life that this material represents. The matter of collecting as large a number as possible of Chinese embryos, fetuses, and abnormal products of conception, must of course be the first consideration in a work of this kind, and will continue to occupy much of the time and attention of the investigators for some time to come. But it is hoped that the time will come, and that not too far removed, when an increasing interest on the part of an enlarging number of contributors will insure an adequate and continuous supply of embryological material from the four corners of China, and the routine of receiving and properly caring for the collection will be in the hands

of a qualified assistant, allowing the laboratory staff to give all its time to the study of the many interesting problems that the material represents.

A detailed report (1) of the collection up to April 1, 1921, is to be found in a recent number of the China Medical Journal, and you are referred to this for detailed information as to the progress already made along the line of collecting and preserving this type of material. For our purpose this morning those features of the work will be reviewed which place special emphasis upon some of the more practical problems involved.

The complete list of specimens at the end of the report referred to above and more particularly the appended summary of the list by individuals, seeks to give credit to each person who has contributed to the collection. A casual analysis of a revised summary of those contributors reveals the significant fact that of the 187 specimens, 135, or 72 per cent, have come from women physicians. It is also interesting to note further that of the entire number of specimens in the collection, 114, or considerably more than half of the whole collection, have come from the large clinics of only four women medical missionaries.

These facts are mentioned here because they emphasize not only the degree to which the women physicians of China are today in practical touch with an important field of medical work which still remains very largely closed to medical missionaries of the opposite sex, but also, evidenced by the four women who have furnished more than half of the entire collection from the material of their four respective clinics, the fact that the difficulties in the way of building up a large maternity work among the Chinese women are not as insuperable as is usually supposed. The evidence of this collection, as well as the personal observations of the writer of this paper during a recent trip among the mission hospitals of Central China, convinces him that where there is a real desire on the part of the physicians in charge of a women's work to enter into this field of needed service; and where tactful announcement and solicitation is made among the large number of pregnant women who come to the daily clinics for the treatment of other conditions, but who would in the natural run of events go as a matter of course to a Chinese midwife to be multilated at their time of confinement, there is a ready and grateful response.

EMBRYOLOGICAL RESEARCH IN CHINA

So much for the general points of interest connected with the collection and some of the implications which an analysis of the sources of the specimens makes possible. We turn now to "Some Practical Aspects of Embryological Research in China."

We are dealing in the last analysis with those products of conception among the Chinese which, usually through imperfect development or maldevelopment, or because of an abnormal or diseased environment, or because of artificial interference, or for any other reason, fail to pass safely through the normal period of gestation and become new normal living individuals. The problems associated therewith reduce themselves into the determination of the rate of prenatal death among the Chinese, an investigation into its causes, and the subsequent invention of means towards its prevention. Of these, the first two naturally take precedence over the third, and it is with these that the work under consideration is at present concerned.

The difficulties in arriving at an accurate conclusion concerning the frequency of abortion among any people increase proportionately as these people are removed from scientific medicine. Statistics along this line in America are just now becoming available, yielding estimates of one abortion for from every 2.3 Taussig (2) labors to every 5 Williams (3) labors. Of conditions in Europe, Franz (4) places the figure for abortions at 15.4 per cent in a typical lying-in hospital in Germany, Malins (5) reports 19.23 per cent of abortions in a representative series of 2,000 pregnacies in England, while Ballantyne (6) quotes Tarnier and Budin (7) to substantiate his claim that throughout Europe in general the fetus at the beginning of intra-uterine life runs about a 25 per cent risk of never reaching the time of viability. With the possible exception of that of Taussig, all of the above estimates are admittedly too low, failing to take into account very early abortions as well as an estimation of those cases failing to come into the hands of medical practitioners. To the above is to be added, by deduction in the case of the human, a percentage of normal prenatal deaths, with degeneration and absorption of the early zygote, which is now known to exist in the case of all animals studied. Robinson (8), who has contributed most to our very recent knowledge of this factor, estimates that this normal prenatal death rate in the human family under our present conditions of living amounts to over 40 per cent. This figure, though purely speculative in the case of the human, is nevertheless a very conservative estimate according to our more definite knowledge of conditions in other forms.

Turning now to specific inquiries along similar lines among the Chinese, it is only reasonable to expect that the prenatal death-rate here, both the normal which we have just mentioned and the more or less avoidable abortions with which we meet more commonly, will be found to be not less high than in Western groups of the human family. A careful study of accumulating records will be necessary in order to arrive at accurate conclusions concerning these questions. This is obviously a matter for the future, but it serves our purpose today to emphasize the importance of these records at this time of early beginning, as well as to indicate a few of the specific lines of inquiry upon which it is desirable that they contain data.

CAUSES OF EARLY ABORTIONS

Spontaneous expulsion of the ovum in the early weeks of pregnancy is invariably accompanied or caused by fetal death, and, as Williams (3) points out, any consideration of the etiology of abortion in this stage resolves itself practically into determining the cause of the fetal death. Mall (9) in turn maintains that a very large percentage of these early fetal deaths is due to abnormalities of development which are usually inconsistent with life. Had these lived on, as is sometimes the case, they would have produced one of the several types of monster which are not infrequently seen. As to the factors directly concerned with the production of these abnormalities of development, the student finds an endless contradiction of opinions. Mechanical, toxemic, microbic, and toxic agents, have each and all been invoked as explanatory causes. Aside from the abnormalities in the development of the embryo itself, Mall's studies showed further that abortions at this early stage resulted also from abnormalities in the fetal appendages which interfere with the nutrition of the fetus (9). Serious studies into the causes of these early

degenerative and abnormal developmental changes in forms other than human have been carried out along the lines of the condition and health of the parents; the environment and food of the parents; the age of the parents; excessive service on the part of the male; the health of the environment of the gametes and the resulting zygotes; the nutrition of the fertilized ovum, and the constitution of the gametes, and the possibilities of individual variations therein conducive to incompatibility in the case of certain matings (8). Although the results of these investigations have so far been scant from the standpoint of positive knowledge gained, yet the list of factors considered is suggestive. Among some of the lower classes of the Chinese such factors as the health of the women, early and frequently incompatible marriages, marital unhappiness, frequent hysterical fits of unrestrained anger on the part of the women in the home, probable excessive intercourse, the practice of prolonging lactation to avoid pregnancy, and other causes, suggest themselves as possible factors in this subtle problem of the failure of many early ova to develop and their subsequent expulsion.

Demonstrable abnormalities in the generative tract of the female, arrested development or infantilism, malpositions of otherwise normally formed organs, chronic metritis secondary either to malposition or to infection, any other conditions bringing about circumstances unfavorable to implantation and later nutrition of the ovum, may be expected to account for their share of early abortions in China as well as elsewhere. These physical and pathological factors in the generative tract of the mother, although belonging more strictly to the gynecologist than to the embryologist, are nevertheless factors which will have a direct bearing upon the results of the present studies if they are found to exist with disproportionate frequency among the Chinese. Taken by and large, it is hardly to be expected that special conditions in China will add to or subtract from the number of fundamental factors concerned in these early abortions, yet the detailed study of the embryo, sac, chorion, decidua, and uterus in as many cases as possible cannot fail to add to our general knowledge of this difficult subject, and help to clear away the clouds that so envelop it in mystery at the present time.

CAUSES OF LATER ABORTIONS

Passing on to the consideration of abortions and miscarriages in the later months of pregnancy, we feel ourselves upon more solid ground and in possession of more tangible facts. What are some of the questions which a study of the records and of the specimens themselves ought to answer?

In contradistinction to the abortions of the earlier weeks of pregnancy, these later abortions are usually due to interference with the placental circulation of the fetus through disease or abnormal development of the decidua, and not to the death of the fetus *per se*. The physical and pathological conditions of the female generative tract that have just been mentioned in connection with early abortions may also exert a latent influence and constitute the predisposing cause of abortions in the later months. Infectious diseases, either by the transmission of toxins or less frequently the specific organism itself from mother to child, may be expected to act in China as elsewhere as a factor in the production of abortions. In Central and Southern China, Dr. J. P. Maxwell has found that malaria is a causative factor in a very large percentage of abortions every year; these may be

prevented, however, by the prophylactic administration of 4 to 5 grains of quinine daily to all pregnant women throughout their term of pregnancy.

The rapid spread of syphilis throughout China, especially in the port cities and along the projecting railroad lines, offers a unique opportunity for the study of the relative frequency of late abortions in regions as yet practically free from the disease as compared with those already infected. The influence of plagues and famines, and the resulting malnutrition and bone diseases, especially the osteomalacia of Shansi and Kansu, the possible effects of foot binding on the development and shape of the female pelvis, and other factors suggest themselves as worthy of investigation in connection with the larger problems of the prenatal death-rate of the Chinese.

Observations along most of these lines have already been started. In connection with questions of nutrition, famine, maternal syphilis, and foot binding, we must not fail to mention the unique opportunity to investigate the effects of these factors which was afforded by the large work of Drs. Jean I. Dow and Isabelle McTavish of Changteh, Honan, when they delivered and cared for nearly five hundred babies from among the women of the famine district during the winter of 1921. It is to be hoped that complete reports of this unique service will soon be available.

CONCLUSION

The general trend of this paper has purposely been almost entirely suggestive in nature. The work which we have ventured to bring to your attention is not of a type which can be carried on by any one single investigator or by any one isolated laboratory. Most of the questions suggested await for their solution the gathering of a very much larger number of specimens, and the studies of many more investigators working on the material in this and in other collections and on the records thereof. It is to be hoped that an increasing number of medical men and women in China will find an opportunity to spend longer or shorter periods of time in laboratories, working on some of these problems and making definite contributions to our knowledge and the literature of the subject. Such work, as suggested in the preliminary report referred to above (1), ought to provide not only a pleasant vacation to a medical worker, but at the same time furnish a distinct contribution to the scientific study of conditions among the Chinese people.

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DEPARTMENT OF PATHOLOGY

INCLUDING JOINT SESSIONS WITH THE

DEPARTMENT OF SURGERY

PRESENT DAY ASPECTS OF PARASITOLOGY IN CHINA

By

ERNEST C. FAUST, PH.D.

Several epochal discoveries in medical parasitology have been contributed by workers in China on Chinese material. *Fasciolopsis buski*, the large intestinal fluke of man, is peculiarly a parasite of the Chinese, with a special endemic area in Chekiang Province. *Clonorchis sinensis* was first recovered from the liver of a Chinese. Although *Schistosoma japonicum* was first described from Japan, it was being studied contemporaneously by Logan at Changteh. One needs only to mention the great stimulus to life history investigation produced by Sir Patrick Manson, at the time working in Amoy, on the periodicity of *Filaria bancrofti*. A more recent species, *Filaria circumocularis*, has been described from the eye of man and of the dog from North China, Fukien, and has likewise been found in Anhwei.

In spite of this work, the vastness of the country, coupled with the need for first-aid for the suffering millions of China, has prevented the development of medical parasitology as the subject warrants. For that reason surveys to determine the extent of parasitic infections in particular areas are illuminating in identifying the parasitic species present, the extent of infection of each species, the life histories of such parasites, and the pathological pictures of each infection.

Various methods are suggested for approaching the problems involved. Routine examinations carried on in the clinical laboratories of hospitals in strategic centers provide a helpful basis for determining such parasitoses. But they are frequently inadequate, due to lack of time and insufficient preparation on the part of laboratory technicians. Intensive examinations covering the same areas are much more fruitful. These may be conducted for stated periods to determine the incidence of infection and to secure samplings of the whole population or of particular groups. When these data are supplemented by information on the infection of domestic animals acting as reservoirs of human parasites and of animals acting as intermediate hosts of such parasites the data are even more suggestive. Such a survey indicates a much greater prevalence of protozoa and helminths as actual and potential parasites of man than ordinary examinations reveal.

In certain areas of China parasitic infections are of primary clinical importance; in other areas they are incidental. The state of our present knowledge leads one to divide China into two climatic regions, arid North China and the moist regions of the Yangtze Valley, and the South. In the former, amœbic dysentery, kala azar, tertian malaria, echinococcosis, ascariasis, and ankylostomiasis are diseases which compel the attention of the clinician. In the Yangtze Valley, amœbiasis, giardiasis, tertian, quartan, and estivo-autumnal malarias, bronchial spirochetosis, fluke infections, ascariasis, ankylostomiasis, and filariasis are all frequently found as primary agents of disease. Because of climatic conditions in the Yangtze Valley, schistosomiasis, clonorchiasis, and fasciolopsiasis are important pathogens.

In addition to the parasites mentioned there are some which occur occasionally as primary agents of disease and others commonly found but not regarded as provoking a severe pathological condition.

The increased interest on the part of practitioners, coupled with the widened viewpoint in medical parasitology due to the introduction into this field of specific protein sensitization tests, culture methods, and new theories of therapy, and particularly the relating of clinical symptoms to life histories, make the prospects bright for parasitology in China.

ACCOMPANYING DEMONSTRATIONS

1. Common parasites of the Yangtze Valley.
2. *Virofilaria immitis.*
    - *a.* Gross specimen in heart.
    - *b.* Immature larvæ.
    - *c.* Mature larvæ.
3. Variations in *Fasciolopsis*, human and hog.
4. *Schistosoma japonicum.*
    - *a.* Mature Worms ♂ and ♀.
    - *b.* Mollusc host in Japan.
    - *c.* Gross organs from postmortem.
    - *d.* Sections of liver showing cirrhosis.
5. *Clonorchis.*
    - *a.* Tissue of liver showing pathology.
    - *b.* Egg.
    - *c.* Gross pathology, cat, dog.
    - *d.* Specimen from cat, dog.
    - *e.* Human case.
6. Malaria.
    - *a.* Estivo-autumnal, premortem and postmortem.
    - *b.* Tertian.
7. *Embadomonas sinensis*, nov. spec.
8. *Spiroschaudinnia.*
    - *a. Carteri*, from blood.
    - *b. Eurygyrata*, from feces.
    - *c. Bronchialis*, from sputum.
9. *Gnathostome* from cat.
10. *Filaria* from ant-eater.
    - *a.* View of animal.
    - *b.* Stereogram of pathological picture in liver.
    - *c.* Demonstration of worms.
11. *Echinococcus* from liver of man.

Autopsy Room, Pathology Building

Parasitology Laboratory, Pathology Building

CERTAIN ASPECTS OF PARASITOLOGY IN THE PHILIPPINES

By

Frank G. Haughwout, M.D.

Gentlemen:

In beginning this talk I feel I must apologize to you for its exceedingly sketchy nature, for until I arrived in Peking I had no intimation that I was to address you. We must blame that on the fact that the letter informing me of this passed by me as I was en route between Manila and Peking. So now I must add to the admiration and delight that your hospitality and this beautiful plant have awakened in me, the pleasure of presenting a few of my hobbies to you.

The work in tropical medicine in the Philippine Islands was organized on an extensive scale years ago, and soon after, a series of surveys was undertaken with the idea of outlining the problems involved. This was done very well as far as it went. Then evil days fell upon the Philippine Islands. Since 1913–14 practically no productive work has been done along any of those lines, and today the problems of parasitology must be re-undertaken.

We are now at the close of the spectacular era in tropical medicine, the era that was exemplified by the work of Laveran, Manson, Ross, and other men of that group. We were able to build on the foundations laid by these men and to develop the science on a sanitary and curative basis. As a result, the present nature of the problems is more distinctly biological and demands the work of the pure scientist. While it would doubtless be dull and dreary work for the clinical man, it is to my mind the dawn of a new day for the worker in pure science along parasitologic lines. With regard to my own work in Manila, I imagine that my position is similar to that of Dr. Faust here in Peking, in that I have to handle practically the whole department of parasitology.

There are a number of interesting problems to be worked out in this connection. This morning, however, I wish to deal particularly with the question of intestinal infections, with merely a passing word in regard to the general types of parasites found in the Philippines and the diseases for which they are responsible. These are much the same as in other tropical countries. We are fortunate in escaping many diseases of the tropics, such as kala azar and those due to some of the spirochetoses. We have the intestinal spirochetal infections, but they are apparently not pathogenic, and this field is restricted largely to the luetic and yaws infections. *Spirochaudinnia bronchialis* occasionally is found. We also frequently come across skin ulcers where search reveals spirochetes and fusiform bacilli. We have, of course, the malarial and helminthal infections. The general run of intestinal flagellates are found, such as *Trichomonas*, *Chilomastix*, and *Giardia*, and very recently I have found the sporozoan parasite, *Isospora hominis*. Among the ciliated protozoa is *Balantidium coli*, but this is not common. A very important group of protozoa includes the intestinal amœbæ, *Entamœba histolytica*, *Entamœba coli*, *Endolimax nana*, *Dientamœba fragilis*, and *Iodamœba butschlii*. I reserve judgment on the last named organism because I have not had an opportunity to study it thoroughly.

In the study of human parasitism we miss much by the neglect of the factors of evolution. We fail to consider our parasites as strictly as we should from a biological standpoint. In this part of the world we are driven to deal with prevailing conditions, and we seek first, of course, to relieve clinical symptoms. This had led us in the past to a sort of empiricism in parasitology that has held back the science to a considerable degree. A remark made by Dr. Faust yesterday morning bears very closely on this point, and I agree with him that we should make greater efforts to correlate the life cycle phases of our parasites with the symptoms of the diseases they produce. Great advances would be made in the treatment of disorders were it always possible, for example, to administer the necessary drug when it would be most efficacious, that is at the most vulnerable period in the life cycle. In the treatment of malaria, for example, we are accustomed to administer quinine at a time when the blood stream contains the sporulating parasites.

MALARIA

The story of malaria in the Philippine Islands is practically the same as in other tropical countries. The disease presents the same recurring symptoms and follows the same general course. All three types are found, tertian, quartan, and estivo-autumnal. The prevailing type is probably the estivo-autumnal, but benign tertian infections are very common, and not infrequently both infections are found in a single patient.

One of our most interesting problems, however, is in connection with malaria. For many years we flattered ourselves that we knew everything about the life cycle of the plasmodium of malaria; but we have yet to determine the cause of malarial latency and relapses; what conditions exist within the human host that lead to the persistence of the infection over long periods of time and what conditions supervene to break down the resistance of the host — and incidentally what the parasite has been doing all that time.

THE HELMINTHS

With regard to the helminths: The records show only one indigenous trematode in the Philippines, the *Echinostoma ilocanum*, reported originally by Garrison (1) from a rather restricted area north of Manila. It was subsequently investigated by Hilario and Wharton (2), but in no case was it possible to work out the life cycle. Our helminthal infections are largely restricted to the nematodes. *Trichuris* is probably the most common of the helminths found in the intestinal tract. In a series of subjects which I studied it was present in 69 per cent. *Ascaris* is also exceedingly common, particularly in children, where the infections occasionally reach a very massive stage and are quite similar to those here in China. Filariasis is present in several localities. For the most part the larvæ do not show diurnal periodicity in the blood, and elephantiasis is almost unknown. Among the cestodes, *Tænia saginata* is probably the prevailing species, but more research is needed in this direction. Occasionally we get an infection with *Hymenolepis nana*.

The incidence of hookworm in the Philippines varies with the locality, and this problem is at present undefined. Much work has been done on hookworm infections, but there is apparently no record as to the probable distribution of the species. It is very important for us to know something regarding the dominant

species of hookworm. In my opinion, it is probably the *Necator americanus*. Heretofore, hookworm investigation in the Philippines was considered relatively unimportant, partly because, although the disease was more or less prevalent, the natives did not seem to be seriously affected by the parasite. Many immigrants, however, from China and Malaysia are apparently importing ankylostomiasis, and a large number of the American population have become infected with the disease. Consequently, unless care is exercised, serious trouble seems imminent.

THE FLAGELLATES

A question of vital importance bears upon the pathogenicity of the intestinal flagellates. Although the literature on this subject is enormous, direct evidence in regard to the matter is almost totally lacking. Personally, I regard these flagellates as a separate race of protozoan organisms, like other intestinal parasites of pathogenic significance, pursuing their course entirely apart from any other living organism in the intestine. One thing that impresses me very sharply in regard to them is that an apparent process of evolution appears to be taking place in one group in particular, the trichomonads. I have seen these organisms appear in stools under all circumstances. Frequently in the passages of bacillary dysentery, I have encountered them swimming about among the blood corpuscles without ingesting any of them whatever. On the other hand, there have been instances of similar physical conditions where trichomonad flagellates ingested blood corpuscles and digested them. This to me, is a very strong indication of a growing adaptation in certain races of these flagellates to obligatory tissue parasitism. Hadley (3) has taken up this problem in some of the lower animals and has described a method of invasion of the intestinal mucosa through the goblet cells. More recently Wenyon (4) has described his findings in a man in India, where precisely the same performance has apparently taken place.

While it is barely possible that this invasion takes place under conditions supervening immediately after the death of the patient, I doubt it very much because the invasion is too deep. I doubt it all the more because within the past year I have had an opportunity to study a case of trichomonad infection of the pleura in a Chinese in Manila. The organisms recovered from the pleural exudate were unquestionably trichomonads of the type found within the intestinal tract. They undoubtedly reached the pleura by way of the blood-stream, although direct evidence of this fact is lacking. However, if the case proved nothing else, it proved at least that trichomonad flagellates of a distinctly intestinal type are capable of living in other parts of the body. That, to my mind, is added evidence of the possible evolution of the race of these parasites towards obligatory tissue parasitism.

COCCIDIOSIS

A recent investigation of interest has been made in regard to human coccidiosis. Up to the time of the war, the literature on this infection had been in a very chaotic state. In 1915, the laboratory work of the British and French was organized on an extensive basis, under such able protozoologists as Colonel Wenyon, Professor Dobell, Colonel Woodcock, and others. One of the first discoveries made was that of coccidiosis in man, in a soldier invalided home from Mesopotamia. In the feces a cyst of *Isospora* was recognized. Other cases were observed, and

they all came from a strip of land running southeasterly from the Balkans, across the Mediterranean, down into Mesopotamia. Castellani (5), in 1917, reported coccidiosis as common in the Balkans. During the next two or three years new species of human coccidia were definitely reported and studied. These included *Eimeria wenyoni*, *Eimeria oxyspora*, and *Isospora hominis*. Subsequently Snijders (6), in Java, reported an isolated case of still another species, now known as *Eimeria snijdersi*. With this exception the endemic area of all the species centered around Mesopotamia, and cases of the disease which appeared in other parts of the world were almost all traced to that locality. Four of the cases, however, encountered in New York City were in the Home Service Troops, which raises some suspicion of their being autochthonous.

A case of infection with *Isospora*, the European coccidiosis, came under my own observation in Manila in 1921 (7). I was tremendously interested because I had predicted in 1917 that this very thing would happen. The man's history revealed that he had been associated in the United States with soldiers returned from the war and with laborers drawn from the Eastern Mediterranean area. His infection lasted at least four months, because he was still infected when I sent him back to the States. During his stay in the Philippines he traveled through a very wild and insanitary district in Mindanao. It will therefore be very interesting to discover whether this infection spreads in that region in the future.

It is difficult to know just how to treat these cases of coccidiosis. Ipecac, emetin, thymol, and salvarsan have been tried without results. The parasite, as you know, is an epithelial cell parasite probably of the upper intestinal tract. This suggests again the question of life cycle and treatment mentioned by Dr. Faust. We cannot treat these cases logically without regard to the life cycle of the infecting organism. The treatment of coccidiosis in man should rest on much the same principle as the treatment of malaria. I regard the chances of effecting cures in these cases as remote at best, and we cannot accomplish anything at all unless the drug reaches the bowel at the time when conditions are most suitable; that is, when sporulation is taking place. The difficulty here lies in determining when multiplication or schizogony takes place and when the merozoites are formed. It was rather significant in the case I have cited that there was a definite tertiary periodicity in the character of the stools, which to my mind is possibly indicative of the period of merozoite formation.

BALANTIDIAL INFECTIONS

The balantidial problem is one that is particularly interesting to me from the zoological standpoint. Little is known regarding the life cycle of the *Balantidium coli*. Several years ago Walker (8) made a study of balantidial infections in man and also in the pig, and he concluded at that time that most of the human infections came from local pigs. The infestation of pigs in Manila by this parasite is very large, quite as large, I imagine, as it is in some parts of China. Dobell (9), however, in the course of extensive studies in England, failed to find a single case of balantidial infestation in man, whereas the pigs are heavily infested. This raises the whole question of species. In my opinion the species of the pig host is not the same in England as it is in the Philippine Islands. Moreover, the infestation in American and British pigs is said to be confined to the lumen of the bowel. In pigs

in the Philippines, however, the *Balantidium* penetrates the mucosa and comes to rest in the submucosa, behaving in precisely a similar manner in both the pig host and the human host. But it is strange to note that in pigs we frequently recover *Balantidium* in the encysted form, while in human infections cysts are very rarely found. Dr. Walker in his series of cases was fortunate enough to find two or three instances of encystation, but I myself, have never found a cyst in human feces. I am, therefore, inclined to believe that the *Balantidium* is specifically a parasite of the pig in the Philippine Islands with rather incomplete adaptation to the human host.

We miss a great many balantidial infections because of the absence of clinical symptoms that are characteristic of acute balantidial infections; but occasionally we come upon a frank case of balantidial dysentery. Not infrequently the patient does not survive the attack, and we have an opportunity to study the case at autopsy. We find the organism in the intestinal wall accompanied by much the same lack of tissue reaction as we see in uncomplicated cases of amœbic dysentery. The picture is similar clinically, pathologically, and parasitically.

DYSENTERY

Ignorance as to the contributing cause of acute amœbic dysentery is one of the most baffling problems that confront us. It is known that the amœba may inhabit certain parts of the human body, principally the submucosa of the large intestine. It usually stays there, and, in a large proportion of cases, causes no damage, but suddenly in some instances, it precipitates an attack of amœbic dysentery through conditions of which we have no information.

Our knowledge of the life cycle of the amœba is not complete. We know that it forms cysts which serve as the agents of transmission of the organism from host to host. The cysts are passed with the bowel discharges and are relatively resistant to environmental conditions. I say relatively, because they do resist the action of chemical agents of a strength greater than those ordinarily present in food substances or in drinking water. They do not resist the influence of bacteria in concentrated growth nor of desiccation, but they do resist the ordinary conditions that prevail. If the cyst leaves the intestine in its fully developed stage it is, barring accident, capable of infecting a new host. It is my belief that the most frequent method of infection for this organism is through the medium of carriers, mainly contact carriers. I think that the chances of infection through the drinking water are relatively slight; that it does occasionally take place, but that it is not the most frequent mode of infection. Fly transmission is, I believe, very important.

The cysts enter the intestine of a new human host, pass through the stomach, and enter the small intestine, and there for a time we lose track of them. It is a more or less generally accepted belief that these cysts open in the small intestine under the influence of the digestive juices there. I do not consider that this point has been proved by any means, however. We have knowledge of the life cycles of many free living protozoa, and we know that in many cases those species that form cysts leave their cysts not through the direct influence of environmental conditions, but by reason of causes wholly within themselves, the whole thing being precipitated, as it were, by an external stimulus of some kind. I am inclined to believe that such a process does take place in the case of *Entamœba histolytica*

which, as is well known, is an obligatory parasite of the large intestine, not of the small. If these cysts open in the small intestine the amœba within them, which are obligatory tissue parasites and are incapable of digesting any other food than they find in the intestinal tissue, have a long journey down to their definitive site. Ultimately, however, the amœbæ arrive in the large intestine, and a certain proportion of them leave the cysts, whether in a mononuclear or quadrinuclear state, I cannot say. They penetrate the intestinal mucosa and rest in the submucosa, probably causing relatively little damage. They make their way rather rapidly to the submucosa, where they stay. They feed on what they find there, and consequently reproduce, and in the course of time the infection becomes rather intense. I am of the belief that in the very early stages of these infections cyst formation does not take place, but in due course of time it begins. It may be a week or two, or even longer, before we detect it. The time arrives, however, when it is necessary to establish a balance between the host and the amœba. This balance is maintained when cyst formation begins and a certain proportion of the amœbæ give up their trophic life, that is, the life in which they are digesting and ingesting food. They then become physiologically transformed. Probably at that period when physiological transformation is beginning they pass out into the intestinal lumen and become morphologically transformed. Effete matter, food that has been accumulated, and a certain proportion of water are expelled. The amœba rounds out and the animal assumes the precystic form. Shortly afterwards it encysts.

It is true that possibly some condition may supervene within the host that leads to suppression of cyst formation. If this takes place one can readily see that the tissue will become overrun by amœbæ, and mechanical pressure will bring about a process that will ultimately lead to ulcerative developments. It may be that the endocrine system exerts some influence. There may occur from time to time in the host the removal of some inhibitory influence or the development of some stimulating influence that will bring about the reproduction of the amœba at a rate more rapid than can be compensated for by the normal reparative processes of the host.

A point I had not intended to take up this morning was suggested by a casual remark by Dr. Mills. This is in regard to the value of the microscope in the diagnosis of both amœbic and bacillary dysentery. I am a strong advocate of the use of the microscope, but long experience has taught me that in dealing with intestinal infections, the microscopist should be in very close harmony with the clinical man. In Manila, at present, we make our diagnoses of dysentery, no matter what the type, by the microscope. I usually check this, because I am collecting statistics, with the findings of the bacteriologist, who at best is working under great disadvantages; but I no longer rely upon his methods, for I believe that in the majority of cases an experienced man can make a very accurate differential diagnosis under the microscope very soon after the patient comes in for treatment; whereas if we wait for the bacteriological diagnosis we are fighting against fate, we are possibly going to lose, and the patient may die if he has an acute dysentery.

During the late war, a very excellent paper was published by Willmore and Shearman (10), in which they assembled and summarized much information

regarding the cytology of the dysentery stool that many of us, especially in the tropics, had known in a vague and general way for years. Wenyon and O'Connor (11) have taken up very much the same subject, and later Woodcock (12) summarized the matter; so that the ground has been covered very thoroughly.

Briefly, in the general run of dysentery cases, the bowel exudate is more or less characteristic of the type of dysentery, particularly in protozoan and bacillary dysenteries. In bacillary dysentery as you know, the onset is apt to be sudden. Very early in the progress of the disease an exudate occurs consisting largely of polymorphonuclear neutrophiles, more or less in a state of disintegration with a great amount of mucus and blood. That in general is the characteristic stool of bacillary dysentery. But there are other considerations. For instance, careful study of the stool, will sometimes show that a so-called "amœbic dysentery" is what I might characterize as an "amœbic dysentery of the endothelial cell type." In other words, it is bacillary dysentery. Examination will show that cells of the mononuclear type are almost completely lacking. Moreover, there will be abundant epithelial cells, endothelial cells, and macrophages, many of which unfortunately have been mistaken for amœbæ by inexperienced workers and the cases labelled "amœbic dysentery." But these stools, in frank bacillary dysentery, bear the stamp of toxic necrosis. There is an abundance of the large macrophage cells, not infrequently containing red blood corpuscles, which cannot be mistaken after they have been seen a few times.

A few months ago I was called upon to investigate an alleged epidemic of amœbic dysentery. I was more or less skeptical, because I have no great belief in epidemics of amœbic dysentery. Before I had been a week at the seat of the trouble I felt that this outbreak was not amœbic dysentery at all but a dysentery of the "endothelial cell type" just described. It was finally shown that it was a bacillary dysentery of the Flexner type. A similar instance occurred in the British Army in Mesopotamia.

Another great source of trouble for us in the tropics is the prevailing opinion of the man who comes out from the United States to work that there are two types of dysentery. One of these is amœbic dysentery, characterized by the presence of amœbæ and by the lack of pyrexia and symptoms of toxemia; the other is bacillary dysentery, with an elevation of temperature to 101° to 104° F., symptoms of toxemia, collapse, and all the other symptoms of severe dysentery. Such general clinical diagnoses often give rise to mistakes.

During the past year or two there have been numerous cases of dysentery among our staff in the Bureau of Science in Manila, and the following routine has proved very successful in their treatment: The patient wakes up at about three or four o'clock in the morning, develops cramps, and soon begins to have rather large bowel movements. He comes to the building in time to report, and is sent down to my laboratory, where a fresh specimen is examined under the microscope. The picture is usually absolutely characteristic of bacillary dysentery. I give the man a note to the serological laboratory, where he is injected with 20 or 30 cc. of polyvalent antidysenteric serum. Then he goes home, goes to bed, with a hot water bottle over his abdomen, and in the majority of instances reports for duty on the following day. That man has had bacillary dysentery, but it has been controlled very quickly. He has shown his symptoms and has come in promptly; we have

made the diagnosis under the microscope and have given him his serum at the very time when he should receive it. If we had waited for the bacteriologist to make a diagnosis, the patient would have become much worse. These cases show at most only a slight elevation of temperature and no toxemia or collapse.

All cases of bacillary dysentery are not always satisfactory after the first thirty-six hours. But in the general run of Flexner infections the patient will show very slight or no febrile symptoms, no signs of collapse, no signs of toxemia. On culturing the stools of such cases, in most instances it is shown that the organism present is a bacillus of the Flexner type. Out of hundreds of cases of this description that I have seen in the Philippines, many have been diagnosed clinically and microscopically as amœbic dysentery. We therefore cannot be too careful in our diagnoses of amœbic dysentery, and I lay down this fundamental principle to my students and assistants: "Be very careful of a diagnosis of amœbic dysentery in the absence of amœbæ." An experienced man will have little difficulty in diagnosing microscopically acute dysentery of the usual types — I am not speaking of the clinical diagnosis. An acute case of dysentery should not be missed, and if the onset is protozoan in character, the organism should be found. In my own experience *Entamœba coli* is seldom encountered in a stool of a case of well-established acute amœbic dysentery. Lumen-dwelling protozoa usually disappear early in the attack, with the exception of certain of the flagellates, some of which will persist in crypts and appear throughout the course of a long attack. In the early stages of the disease it may be possible to check the diagnosis. The stool may consist of two very definite portions, a fecal portion and a bloody-mucoid portion. In the latter amœbæ containing red blood corpuscles are frequently recovered, and they may be said to constitute a diagnosis of entamœbic dysentery. A mild controvesy is going on in regard to this point, but until we have more definite information I think we are entirely justified in considering the presence of erythrocytes in amœbæ as a very important diagnostic feature. In the fecal portion, encysted forms are not uncommonly recovered. These furnish a check upon the motile forms. Macroscopically the stool may not be dissimilar from the stool of bacillary dysentery. Personally I do not consider it safe to inspect a stool without the microscope, and pronounce it a stool of bacillary or of amœbic dysentery as the case may be. Microscopically in amœbic dysentery you will find mucus and blood. In the primary cases you will notice the seeming, indeed the actual, absence of polymorphonuclear leucocytes. The cellular exudate will be very scant. As the case progresses a secondary bacterial infection may take place, when pus is very apt to appear. Such cellular elements as are present in the early stages consist mainly of cells of the mononuclear type, and in early uncomplicated cases there is a total absence, in the cellular exudate, of any evidence of toxic necrosis. Epithelial cells and ghost cells are lacking. Above all, if *Entamœba hystolytica* is present, it will clinch the diagnosis. That, in a general way, is the fundamental picture, but as I have said before, conditions are frequently very misleading, and the greatest care must be exercised.

Among various misleading conditions which may lead to wrong diagnoses, is the so-called "chronic bacillary dysentery," resulting from carelessness from a post-dysentery standpoint. I myself am skeptical as to the existence of chronic bacillary dysentery. The majority of patients of this class that I see are Europeans

from whom it is relatively simple to obtain exact information. Examination reveals stools laden with amœbæ, possibly with *Entamœba coli*, and in many such cases the collection of pus cells is prominent. The feces may be formed but contains stands of mucus filled with pus cells and epithelium. Clinically, there is perhaps a slight rise of temperature, bowel movements are frequent, and the patient feels ill. Without proper study such symptoms are misleading. The case might easily be diagnosed as bacillary dysentery, whereas in reality the patient has a chronic ulcerative process somewhere in the lower bowel. Many such cases respond readily to dietary treatment. They seldom, if ever, even under the most rigid technical conditions yield a growth of *Bacillus dysenteriæ;* they are chronic, non-specific, ulcerative processes.

A case that puzzled me very much was, I finally concluded, probably one of mercury poisoning rather than of bacillary dysentery. Although the bowel movements were frequent and characteristic of the latter condition, and the stools were laden with pus, I did not find microphages and the picture of toxic necrosis usual in bacillary dysentery.

Another interesting case was observed by Major J. E. Ash of the Army Medical Corps, and myself during an investigation into bacillary dysentery and allied conditions in a military hospital. A native soldier who was suffering from pneumonia developed intestinal symptoms. The usual laboratory examination of the stool suggested bacillary dysentery. When the matter was referred to me, however, I felt doubtful. The patient died and an autopsy was made. Cultures taken were negative for dysentery and examination of the colon showed a diphtheritic colitis, probably secondary to the lung involvement. There was absolutely no evidence of amœbic or bacillary dysentery, and yet superficially, because of the presence of the enormous number of leucocytes, the stool resembled that of bacillary dysentery.

A curious condition once occurred in a young child, who did not show any elevation of temperature, but had been passing stools more or less laden down with pus. The case finally reached my laboratory, where by very good fortune I succeeded in finding a clue to the situation. There is in the Philippines a plant called "gabi" (*Colocasia esculentum* Schott). In the latex of this plant there are little capsules about the size and shape of hookworm ova enclosing a collection of sharp-pointed crystals of calcium oxalate. When eaten raw the plant causes intense irritation of the buccal mucous membrane. The stool contained a few of these capsules and a few free oxalate crystals, and subsequent investigation disclosed the fact that the child had chewed gabi. I may add that in the study of the case my identification of the crystals was checked by Professor E. D. Merrill, the botanist.

The question of the cure of amœbic dysentery is purely a clinical matter which I am not particularly qualified to discuss, but I feel that there is a great deal of work to be done in regard to the modus operandi of the drugs used in the treatment. The work goes back to the excellent pioneer work of Vedder in Manila (13). Dale and Dobell (14) have published a very interesting study on the action of ipecac, and its derivatives, particularly emetin and cephalin. They discovered the fact that while the toxicity of emetin *in vitro* was relatively low, that of cephalin on the other hand was quite high. But in treatment the results were absolutely

reversed. Emetin yielded splendid results; cephalin was therapeutically inert. Now, what is the answer?

Ordinarily acute amœbic dysentery is relatively easy to control, except in cases that progress to gangrenous involvement of the intestine, where the patients die very quickly. A number of drugs are very efficacious. Myristica, or nutmeg, yielded splendid results in the hands of Leidy (15). Chaparro amargosa is another drug of promise. I have had some good results with benzyl benzoate, but I do not believe that any of these drugs, with the possible exception of emetin, has a definite amœbicidal action. Many cases seem to respond very favorably to such treatment, but they are often incorrectly diagnosed cases or cases that would be apt to do well under any reasonable form of treatment. Through the action of some drugs the bowel is given a chance to recover itself, but in very few cases can any lethal action on the parasite be shown. In many instances it seems to me the treatment may restore the balance and bring about the resumption of the ordinary conditions by stimulation of encystation of a proportion of the parasites.

An interesting consideration, which was mentioned by Dr. Faust in discussing amœbic dysentery, is the large number of carriers in proportion to the cases that develop acute dysentery. He is absolutely right. One of the most interesting questions today regarding amœbic dysentery is that the proportion of carriers probably far out-numbers the cases that develop acute dysentery. It is not improbable that only 10 per cent of carriers develop acute symptoms. I am inclined to think that the proportion of cases varies with the race, perhaps due to racial adaptation, and that it may be even lower with the Filipinos and Chinese, although higher with the Europeans in this part of the world. Occasionally we have followed cases of infection in both natives and Europeans for several years, where we have had no previous history of dysentery and none of the manifestations of the disease have occurred during the period of observation. It is impossible to tell how such cases may develop, and whether or not they are going to have an amœbic abscess of the liver, or more properly speaking, hepatic amœbiasis. I am of the belief that any carrier should be treated promptly.

INCIDENCE OF PARASITISM

It is a little difficult to discuss the relation of parasites to human beings in the Philippines because the methods of study have changed very radically in the last few years. The early work of such men as Musgrave, Walker, Sellards, and Garrison was of a very high order, but I do not know just how far their records will aid us under present conditions. I think that a large proportion of infections must have been missed, but nevertheless, I found that my own figures regarding the incidence of parasitism in a certain group was 90 per cent, 3 per cent below those of Garrison and Llamas (16) for a similar group. My studies lead me to concur in Garrison's statement that (17): "The population of the Philippines presents a higher percentage of infection with intestinal worms than has ever been definitely reported from any other people and the condition is essentially a chronic one, the results of which manifest themselves indirectly in the general physical impoverishment of the people and the high rate of morbidity and mortality accredited to other diseases."

The study of parasitism in children has been interesting in many respects. Dr.

Horilleno, one of my former students, and I divided a group of 100 children into three small groups in order to study them (18). The first group included children under the age of twelve months, that is, from seven to twelve months. Of that group 66.66 per cent were parasitized and infections were found at seven months. In the second group, composed of children between the ages of one and two years, 73.6 per cent were infected. The total percentage of infected children up to two years was, therefore, 71.4 per cent. In the third group, consisting of children above two years and under thirteen years, 100 per cent were infected, and in many cases there was a multiple parasitism. In more than one instance we found six species of parasites in one child.

A very significant thing, however, although I do not know whether it is an absolute fact, is the seeming rarity of acute amœbic and balantidial dysenteries, even of ordinary infections by these organisms, in children below the age of puberty. Filipino children are susceptible to every conceivable parasite. Their intestines fairly swarm with *Trichomonas*, *Chilomastix*, *Giardia*, and the non-pathogenic amœbæ, but seldom, if ever, do we find *Entamœba histolytica* or *Balantidium coli*. I have seen a few cases of *Entamœba histolytica* infection in children below the age of thirteen years, but only one case of balantidial infection.

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CONFERENCE ON PNEUMONIC PLAGUE

PLAGUE EPIDEMIC IN THE CHINESE EASTERN RAILWAY REGION IN 1920–21

By

P. Lostchiloff, M.D., and G. Tchaplik, M.D.

The epidemic first broke out in the autumn of 1920 in a village near the railway station of Hailar, on the border of inner Mongolia, among Chinese tarabagan trappers. At first seven Chinese in the same "faungza" fell ill and died. Then some Chinese soldiers fell ill after visiting this faungza, and next the family of a railway guard, who lived in the same building with these soldiers. Finally the plague reached the Chinese settlement nearest to the Hailar station. During the first period of the epidemic the plague was exclusively bubonic but with the beginning of the cold season only cases of pneumonic plague were reported.

During the whole period of this epidemic, which lasted from October 20, 1920 to May 27, 1921, the registered number of cases of plague on the territory belonging to the Chinese Eastern Railway was 1,598 cases, and 2,931 dead bodies of plague victims were discovered on this territory. The number of deaths from plague amounted altogether to 4,529 cases: 4,179 Chinese victims, or 92 per cent; and 350 Russians, or 8 per cent.

All those who were affected by the pneumonic form of the plague died on the second or third day of their illness. From among those who had bubonic plague three were cured, including one pregnant woman, who shortly after her recovery, gave birth to a healthy child.

The localities most seriously affected by the plague were the town of Harbin, with a total of 1,748 deaths; the settlement of Manchouli with 1,137 deaths; and the Chalainor Coal Mines with 938 deaths. The plague reached its maximum severity during the months of March and April. The highest per cent of Russian plague victims was registered in the settlement of Manchouli station. These were destitute refugees and soldiers who lived under very unfavorable conditions and, in many instances, were lodging together with poor Chinese. Among the better off and more intelligent classes, both Russian and Chinese, cases of plague have been very rare. Among the Russian Medical Staff the following persons fell ill with plague and died: Dr. Sinitzin, four surgeon-assistants, and twenty-eight orderlies. Dr. Yuan, a Chinese, also fell a victim to this plague epidemic.

As to the bubonic plague, the real source of the first infected cases was not definitely established, but in the last plague outbreak, as in previous outbreaks, the first victims of the bubonic plague are those who had dealt with tarabagans. There has been no positive evidence to prove that the infection spread from articles belonging to those infected with plague or from corpses of the plague victims. A five-day term of quarantine for people who have been in touch with the plague cases should be considered sufficient. Among 2,014 cases of isolated Chinese there was only one case registered where the first symptoms of infection appeared on the sixth day of the isolation. In most cases the incubation period was three days.

There were no definitely specific symptoms of the plague during the epidemic of 1920–21 on the Chinese Eastern Railway. It had the usual symptoms of a heavy septic disease. Meteorological data collected during this epidemic show that two or three days after there had been cold or wet weather, the number of plague cases increased. The probable reason for this is the necessity for the poor Chinese to remain on such days within their dirty, crowded lodgings, which are often already infected.

Since the nature of the plague is known, this disease is no longer a serious menace to men with high standards of hygienic living. The disease spares such people even when they happen to live in localities which are the very centers of epidemic infection. As regards the region of the Transbaikalian and Mongolian Steppes, the plague should be considered endemic and connected with plague epizooty among tarabagans. Most convincing proof is given by some cases of bubonic plague which were registered in August, 1921: Two employees of the Chita Railway, each of whom had killed an infected tarabagan and skinned the animal before cooking it, were the first victims of the disease. Almost every autumn at the usual time of tarabagan trapping and hay harvest, either single cases or small epidemics of bubonic plague occur in Transbaikalia and Mongolia. These sometimes, as it happened in 1910 and 1920, develop into heavy epidemics. There is now an outbreak of bubonic plague in the territory of the Chita Railway. From the middle of August up to the first of September six Russians have fallen ill and died. This number includes one of the railway doctors who had operated on a patient with bubo, which proved to be infected with plague.

Recent cases of bubonic plague which have occurred in Transbaikalia, do not permit us to look with confidence upon the near future. Scientific investigations of the real causes of plague epidemics in the Transbaikalian and Mongolian regions ought to be undertaken at once. We dare to hope that the Union Medical College in Peking, so well and richly equipped, will not refuse its assistance in the matter of carrying on these investigations in the epidemic foci of the plague, and will thus help to bring to an end one of the curses of mankind.

Dr. Lostchiloff presented the following supplementary notes:

During the plague epidemics of 1910 and 1920 in the territory of the Chinese Eastern Railway no epizooty of any kind was observed on house rats and mice. At the time of the plague epidemic in Vladivostok in the summer of the current year (1921) seven dead rats were found, which proved upon inspection to be plague-stricken.

Two places must be considered as epidemic foci, namely: the Astrakhan or Kirghiz Steppes, lying northward from the Caspian Sea, and the Transbaikalian and Mongolian Steppes in Siberia. The source and carriers of the plague infection in the Astrakhan Steppes, as proved by the investigations carried on by Professor Zabolotny's Scientific Expedition in 1912, are fleas from local marmots (*Spermophilus citillus*). Being a member of this scientific expedition, I myself observed in these Steppes a number of regions (about 10 square yards each) covered with bodies of dead, plague-stricken marmots. Experiments proved that healthy marmots were devouring these cadavers and becoming infected in turn.

No scientific investigations have yet been made to discover the reasons for the existence of these endemic foci of plague in the Transbaikalian and Mongolian

Steppes, and yet this question is of great importance to China as well as to Russia.

There is no reason for considering the Astrakhan Steppes as the origin of the plague epidemic in China, the two places lying so far from each other and having no direct connection with each other. Up to the present time the plague epidemic in the Astrakhan Steppes has been observed only among nomad Kirgizes, wandering in these Steppes and having no connection with the Russian population. Among the latter only a few cases of plague were reported. As far as I know there was not one case reported in the region lying between the Astrakhan and the Mongolian Steppes, although the last epidemic came from the Mongolian Steppe.

The plague epidemic in Northern Manchouli which took place in 1920–21, as well as the one of the year 1910–11, in places of its most intense developments, had a periodic character, lasting, on the average, about three months and in only two points, on the territory of the Chinese Eastern Railway, namely, in the adjoining settlement, in Manchouli and at the Chalainor Mines. Cases of plague during the epidemic of 1921, having been reduced to a minimum at the end of the third month, became more frequent again owing to new cases brought from other places.

With the coming of the warm season the epidemic of the pneumonic plague in 1921, just as in the year 1911, gradually disappeared everywhere except in Vladivostok, where plague appeared in April and lasted till the month of July. (It can be explained by the considerable humidity of the atmosphere in summer in this seaside town.) The total number of deaths from plague in Vladivostok amounted to 493 Chinese and 9 Russians, and among the latter were 6 persons belonging to the medical staff.

DISCUSSION

Participants:

Dr. Wu Lien Teh
Dr. Charles W. Young
Dr. William H. Welch

Dr. Wu: Both in the wards and in the postmortem room we used the two-tailed gauze and cotton mask, recommended by me and accepted by the International Plague Conference in Mukden, 1911. Our staff wore goggles when in close contact with patients, but often this was impossible because of the moisture which would condense on the glass when entering a warm room from the outside cold (temperatures of $-15°$ to $-30°$ C.). In the postmortem room the operator wore two pairs of gloves so as to minimize accidents. The outer pair was boiled with instruments and pails, but the inner pair was simply disinfected with alcohol.

Splenic punctures were performed with a short pointed knife which had been rubbed with tincture of iodine; this tincture was used also for the skin of the cadaver. From the blood thus obtained cultures were made direct on agar in addition to the usual slides. On all occasions, as few men were employed as possible, and the technique was the simplest consistent with accuracy, because of the great danger to all concerned.

The first case of plague appeared at Harbin on January 22, and the last was diagnosed on May 21. Our first complete postmortem was made on February 27,

and the last on May 21. Altogether forty-three postmortems were made, of which thirty-four were cases of plague. You will see from the table that practically all the early ones (up to May 13) were pulmonary in character, only four being septicemic, of which three were in babies under three years. After that date, all the ten cases except one showed purely septicemic features. This raises the question as to whether this preponderance of septicemic cases towards the end of the epidemic affected in any way its suppression. As I said in my address on September 16, it is quite possible that the organisms passing through pneumonic cases were becoming so virulent that there was little or no time for the patients to develop pulmonary symptoms, and the medium of infection, namely the sputum, was therefore absent. As a consequence, the later victims became less infectious, though invaded by more virulent bacilli, fewer infections took place, and the epidemic gradually died out.

The accompanying table representing results from plague autopsies may be interesting:

	Male	Female	Total	Remarks
Pneumonic	15	6	21	4 were of lobar type and of these, 3 were women.
Septicemic	10	3	13	All 3 female septicemic cases were under 3 years.

One unique case needs mention, that of a still-born infant whose mother was sent to the hospital for plague and gave birth to the baby six hours before she herself died. Postmortems were performed upon both bodies. The baby was full-term, and showed the following conditions: larynx and epiglottis — fine hemorrhages throughout; both lungs — no air, but hemorrhages marked on pleural surface; pericardium — contained some blood; endocardium — showed endocarditis, red points being visible on pulmonary valve; trachea and bronchi — some froth, but no blood; peritoneal cavity — full of blood-stained fluid; gall bladder — hemorrhage on surface; spleen, liver, and kidneys congested; placenta — showed plague bacilli, as did all the organs of the infant. Pure cultures were obtained from all organs examined, viz., heart, pericardial fluid, liver, spleen, lungs, pancreas, tonsils, kidney.

The only bubonic case recorded in Harbin, out of 3,125, occurred in a pregnant Russian woman who had swellings in right femoral region. The baby born two weeks after was well. Hers was the only authentic case that recovered.

The tongue, fauces, larynx, and trachea in almost all cases of plague pneumonia were congested, hemorrhages being frequently present. The trachea and bronchi were inflamed, pink, blood-stained froth in greater or less quantities being found, teeming with plague bacilli.

With regard to pneumonia, the lobular form was more often encountered than

the lobar. Where no pneumonia was present, the most intense congestion, often with hemorrhages, was the rule. Acute pleuritis was often marked but fluid was seldom found in the cavity.

Owing to the belief among certain pathologists that the tonsils were the portals of entry in plague pneumonia, much care was taken by us to study these organs. Although hyperemia was present in almost every case, resulting in more or less enlargement, no special changes were observed, certainly none to justify one in believing that they were the portal of entry of the organisms.

All other organs showed conditions usually encountered in cases of septicemia, though the changes found might be more acute than in other diseases. Certainly the liver often presented an appearance seen in acute yellow atrophy, yellow fatty patches being present which showed rapid degeneration of tissue.

Two unusual facts were noted by us. As pointed out by Strong and Fujinami in 1911, tuberculous subjects were seldom encountered in plague pneumonia at necropsy. Strong made twenty-five postmortems and failed to find any tuberculous lesion. Fujinami recorded twenty-six plague autopsies and found only one case where the lungs were tuberculous. We made thirty-four necropsies on plague cases in 1921 and saw three cases of active tuberculosis, namely, one in the lung, one in the cervical glands, and one in the skin. We should, however, be chary about coming to any definite conclusion in the presence of such evidence.

The second fact observed was the apparent persistence of the thymus in plague as well as in non-plague subjects. For instance our records showed the following facts:

	Plague Cases	Non-Plague Cases
Persistent	17 (60.7 per cent)	2 (40 per cent)
Probably persistent	10 (35.7 ")	2 (40 ")
Absent	1 (3.6 ")	1 (20 ")
Total	28	5

The question of the survival of the thymus among the Chinese deserves investigation and I trust our anatomy and pathology colleagues will look into the matter.

CONDITION AMONG TARABAGANS

As pointed out in my address, we managed to produce experimental plague pneumonia in both the small Mukden marmot (*Spermophilus citillus*) and the large Mongolian marmot or tarabagan (*Arctomys bobac*). The specimens show that the changes in the organs are similar to those observed in human beings, the congested and hemorrhagic fauces, trachea, and lungs. In one animal which lived until the seventeenth day as a contact, when it was killed, white pea-shaped masses were noted all over the lungs, which showed under the microscope only a few *Bacilli pestis*. The presence of this subacute form of plague among these wild rodents will form an interesting study. (Since this demonstration was given, our staff has discovered a tarabagan sick and dead of plague in the wild state, con-

firmed later by bacteriological tests.) In the guinea pig specimen you will note the localized peritoneal abscess produced by first inoculating it with our spore-forming bacillus and then with *Bacillus pestis*. The animal lived until the seventh day, although the control did not survive twenty-four hours. The matter requires further elucidation.

Dr. Young: There are two points to which I wish to call your attention. The first is the distribution of plague as worked out by Dr. Wu Lien Teh, especially from Russian sources. This is to be found in the First Report of the North Manchurian Plague Prevention Service (1). Dr. Wu points out that there have been frequent outbreaks of bubonic or pneumonic plague, or both, all the way from the Caspian Sea to Mongolia and Transbaikalia. The regions mentioned are Astrakhan Uralsk, the Kirghiz Steppes, and Semiretchinsk. Observations in Transbaikalia and Northwestern Manchuria are also given. It seems clear that the whole region stretching across these arid highlands is an endemic center of plague, and from the fact that it occurs among nomadic or semi-nomadic peoples, it would seem likely that the source is a wild rodent. It was from this region that all the recent pneumonic epidemics have appeared. In articles on plague in books, Yunnan is usually named as the endemic center of plague. It is more likely that Yunnan is merely one edge of this great Asiatic endemic area.

The second point is that there is in Li Hsien in Western Shansi a small, limited endemic center of bubonic plague, which antedates the pneumonic epidemic of 1917–18, and in which no pneumonic plague occurred. Dr. Percy T. Watson of Fenchowfu, Shansi, has studied this area for several years. He tells me that the maximum incidence of the disease is in the late summer and autumn, and that he has observed a small pneumonic epidemic here, arising in November. It seems to me that this has great significance in view of the fact that all the pneumonic outbreaks of recent years in Eastern Asia have been winter epidemics. The relation of cold weather and overcrowding to the transmission of pneumonic plague is well recognized. The mortality in this area in Shansi has been very high — about 96 per cent in one season. Dr. Watson is present, and I hope will give us an account of his observations.

Dr. Welch: I recall very well the first outbreak of plague in San Francisco several years ago and the excitement caused by the announcement of Dr. Kinyon's positive diagnosis. The picture of plague as it appeared in devastating epidemics in the middle ages was before the minds of the people. The diagnosis was disputed and the issue figured prominently in the political campaign which was impending. One candidate for governor accepted the diagnosis and the other disputed it, the latter being elected — probably a unique instance of an effort to settle a scientific question by popular vote.

Plague, as is well known, is primarily and essentially an epizootic disease of rodents, making under favorable conditions occasional excursions into the human host, where it appears in nearly all cases as the bubonic type of plague with little or no danger of conveyance from man to man. Experience has demonstrated extraordinary difficulties in eradicating the infection completely from the rodent population, but when the incidence in rodents is reduced to a certain point the danger to human beings under ordinary conditions of living becomes minimal. This is at present the situation among the ground squirrels in the infected area

in California, and I believe also among rodents in the county of Norfolk in England, and in many other parts of the world. It is impossible to say positively to what extent the seaports along the Gulf of Mexico and the Atlantic coast of the United States may harbor occasional plague-infected rats.

I had the opportunity to see something of Dr. McCoy's interesting work in his plague laboratory in San Francisco where thousands of rodents, chiefly rats, were examined, and I was impressed with the wealth of pathological material presented, only a small part of which was he able at the time to utilize. The discovery of the plague-like diseases due to other organisms, particularly that caused by *Bacterium tularense*, has become of much significance.

The problems presented by pneumonic plague are in many ways different from those of bubonic plague, although there appears to be no ascertainable difference in the bacilli in the two types of the disease. A remarkable circumstance appears to be the failure of the occasional secondary pneumonias in the bubonic and the septicemic types of the disease to give rise to primary pneumonic plague in those who appear to be exposed, although the rare accidental laboratory infections in working with cultures have been pneumonic. Still the essential difference between the bubonic and the pneumonic types of plague appears to be the mode of infection in each.

Primary pneumonic plague in contrast with bubonic plague is among the most highly contagious and most uniformly fatal of human diseases, but by way of compensation and again in contrast with the latter it is a fairly controllable disease. The campaigns against pneumonic plague in Manchuria, conducted by Dr. Wu Lien Teh, Dr. Strong, and their colleagues, and more recently in the provinces of Shansi and Shantung by Dr. Young and his co-workers, are among the most interesting and dramatic chapters in modern medical history.

Dr. Wu's report at this conference of the inhibitory action upon the plague bacillus and its effects by certain spore-bearing bacteria is interesting and should lead to further study, especially as to its specificity, as it is well known since Buchner's experiments that foreign proteids of bacterial origin from various sources may influence the pathogenic effects of other bacteria.

Those who have the opportunity should not fail to visit the museum of the Japanese Medical School in Mukden, where there is admirably displayed a unique collection of specimens of the Manchurian pneumonic plague. I was particularly interested when examining these specimens in 1915 to note the characteristic lesions of the mediastinum and the mediastinal and tracheo-bronchial lymph nodes. A certain resemblance of these lesions to those found in some of the severe influenzal pneumonias at our camps in 1918 may have given rise to the erroneous impression that there was some connection between influenza and genuine plague.

May I be permitted just to call attention, à propos of my remarks the other day about the comparative study of epidemics, to the interest attaching in the solution of some of the problems of the spread of plague to the study of the habits of the people in their living, their working, their housing, their superstitions, even as affecting contact with animals, and the influence of the seasons upon living and housing habits.

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CASE REPORTS AND DEMONSTRATIONS

By

Henry E. Meleney, M. D.

CASE I. THROMBOSIS OF THE SUPERIOR PETROSAL SINUS AND MENINGITIS, FOLLOWING ACUTE MASTOIDITIS

Meningitis and thrombosis of the venus sinuses of the dura are two of the complications which occasionally follow acute otitis media and mastoiditis. It is rather uncommon, however, for both these complications to occur in the same case, and it is still more uncommon for them to produce a clinical picture suggesting a localized brain abscess, and yet to present at necropsy no gross connection between the original lesion and either of its complications. It is because of these unusual features that the following case is reported.

History. An American missionary, male, aged twenty-two, was admitted to the Peking Union Medical College Hospital three weeks after having had his right ear-drum opened for an acute otitis media. Purulent discharge from the middle ear had persisted until the time of admission. Roentgen ray examination showed clouding of the right mastoid cells. Culture of the pus from the auditory canal gave only *Staphylococcus albus*. Temperature, pulse, and respiration were normal. There was a history of scarlet fever in childhood and a recent systolic blood pressure of 200 mm. Hg. On admission blood pressure was: systolic 148, diastolic 112. Heart was enlarged to both left and right, radial artery was thickened, urine was normal. White blood cells were 9,450 per cmm.

Operation. A simple mastoidectomy was performed, removing granulations and inflamed bone from the right mastoid cells. Culture from the mastoid cells at the time of operation was sterile, but fifteen days later the discharge from the operative wound yielded hemolytic streptococci in pure culture. Patient was discharged from the hospital seventeen days after operation, still having a slight discharge from the operative wound, but otherwise apparently well. Three days later he developed a severe headache localized to the left temple and was readmitted to the hospital. Headache was somewhat relieved by shrinking the turbinates. The next day he had a blotchy erythematous eruption over his neck and chest, his face was slightly swollen on the right side and was flushed. His neck was not rigid. Temperature was 38.5° C.; white blood cells, 10,950; polymorphonuclear leucocytes, 61 per cent. On the fourth day after admission his headache became general and herpes labialis appeared. On the seventh day after admission the right eyelid became slightly swollen and he complained of pain in the right eyeball. Eye grounds were normal. There was slight pain on flexion of the neck, but no definite stiffness. Spinal fluid was under increased pressure, and contained 14,600 cells per cmm., mostly polymorphonuclear leucocytes. No micro-organisms were found in direct smear or on culture of the spinal fluid. On the tenth day after admission the right pupil was larger than the left and there was a right internal strabismus. Coma developed. A subdural abscess in the right temporal region was suspected, on account of which the skull was trephined above the right ear, but exploration revealed nothing. The patient died that night.

Necropsy was performed fourteen hours after death. On removing the calvarium there was no excess of subdural fluid, but the brain pressed tightly against the dura. A pipette inserted into the right lateral ventricle obtained abundant cloudy yellow fluid, which, on culture, yielded hemolytic streptococci. The sulci of the cerebral cortex were made shallow by the internal pressure, and contained yellow purulent fluid, most abundant on the upper and lateral surfaces of the brain. At the base there was practically no exudate, except between the cerebellum and medulla where there was thick greenish-yellow pus. No abscess was found either within or outside the brain. After fixation the brain was sectioned and showed nothing grossly abnormal except congestion of the blood vessels and dilatation of the ventricles by cloudy fluid.

The blood sinuses of the dura were all normal except the right superior petrosal sinus which contained a thrombus beginning at about its middle and extending mesially nearly to the cavernous sinus. It practically occluded the sinus, but was adherent only to the portion of the sinus adjacent to the temporal bone. At its lateral end it was organized and gray in color; in its mesial portion it was red and friable. Microscopically the organized portion was continuous with the sinus wall, and contained ouly a small area of fibrin. The unorganized portion contained many polymorphonuclear leucocytes, small groups of Gram-positive diplococci, and much necrotic fibrin.

There was no gross opening from either the middle ear or the mastoid cells into the cranial cavity. The tegmen typani was intact. The typanic antrum was large and was connected by a large opening with the mastoid operative wound which was still open. The right middle ear contained only granulation tissue. The left middle ear and antrum, and the accessory sinuses of the skull were normal. The spinal cord was congested and surrounded by cloudy fluid, but there was no purulent exudate about it. The visceral organs were normal except for a mild degree of general arteriosclerosis, slight hypertrophy of the left side of the heart with thickening of the mitral valve, and cloudy swelling of the liver and kidneys. Culture of the heart's blood yielded hemolytic streptococci and *Bacilli coli*.

This case illustrates the fact that no gross connection between the middle ear or mastoid cells, on the one hand, and the dural sinuses or the cranial cavity, on the other, need occur in order to produce a serious complication in either of these locations. The tympanic cavity and antrum send small emissary veins into the superior petrosal sinus, and the lymphatics of these cavities are also connected with the walls of the blood sinuses and indirectly with the meninges. The meningitis in this case was probably produced by lymphatic extension of the infection. Whether the sinus thrombosis was of lymphatic or venous origin is more difficult to determine, but the fact that the oldest (most proximal and organized) portion of the thrombus was apparently sterile suggests that it was not a continuation of a septic thrombus in a tributary vein, but was possibly started by an inflammation of the sinus wall borne from the middle ear or antrum by the lymphatics. Micro-organisms may have been introduced into the propagated distal portion of the thrombus either from the original source of the thrombus or from the blood-stream itself. The general bacteriemia which was revealed at necropsy may have arisen either from this septic thrombus or from the inflamed meninges by way of some other blood-vessel.

A third feature of the case which is clinically important is the long period of time between the subsidence of the acute inflammation of the middle ear and mastoid and the development of the signs of meningitis. The case demonstrates that no case of acute mastoiditis or otitis media is free from the possibility of serious complication until the inflammatory process has entirely subsided, even if that be several weeks after the acute period of the disease.

It is interesting to recall, in connection with the thrombosis of the superior petrosal sinus, the symptoms which were suggestive enough of an abscess beneath the temporal lobe to warrant an exploratory craniotomy. Nine days before death the right side of the face was swollen and red. Six days later the right eyelid became swollen and there was pain in the right eyeball. On the day of death the right pupil was larger than the left and there was right internal strabismus. Lesion of the third cranial nerve causes paralysis of the constrictor pupillæ muscle and therefore dilatation of the pupil. Lesion of the sixth cranial nerve causes paralysis of the external rectus muscle and therefore internal strabismus. The ciliary branch of the ophthalmic division of the fifth nerve is the sensory nerve of the eyeball. Lesion of the fifth nerve might therefore produce a sensation of pain referred to the eyeball. Lesion of the superior maxillary division of the fifth nerve might also by reflex action cause vasomotor disturbances in the region supplied by it, and thus produce redness and swelling of the face and eyelid. Except for the paralysis of the external rectus muscle, which is the only possible evidence of lesion of the small sixth cranial nerve, the above symptoms are of the type which would be produced by a very slight injury or irritation of the nerves involved, not by complete loss of their function. In the present case the thrombosed portion of the superior petrosal sinus was in close proximity to these three nerves. It was directly above and close to the Gasserian ganglion of the fifth cranial nerve. The third nerve passed on the mesial side of it and the sixth nerve below and mesial to it. It is therefore possible that the same inflammatory process which caused the thrombosis of the superior longitudinal sinus, also existed about these nerves, and interfered with their function without producing a demonstrable local lesion in the bone or meninges.

CASE 2. SYNCYTIOMA (ATYPICAL CHORIOMA) OF THE UTERUS, TERMINATED BY ACUTE PERITONITIS

Chorioma, the interesting tumor developing from the ectodermal elements of the chorion of the fetus, is known to vary widely both in clinical course and in gross and microscopical appearance. In many cases it is an extremely malignant tumor, causing extensive local destruction of tissue and metastasizing widely by way of the blood-stream. In other cases, with the early clinical and microscopical appearance much the same, it is cured by curettage, or else spontaneously retrogresses, occasionally even after the appearance of metastasis in the lungs or vagina.

Even the earliest writers on chorioma, especially Marchand (1), recognized the great variation in the course taken by the tumor and the difficulty in determining from the histological examination either of curettings or of specimens removed at operation what the ultimate outcome would be. More recently, however, attempts have been made to classify the various forms of the tumor, (Schmauch (2),

Ewing (3), von Velits (4), R. Meyer (5)), so as to determine, if possible, the criteria on which a surgeon could decide whether hysterectomy were required for a complete cure or whether curettage would suffice. Such a classification has not as yet been relied upon to any great extent, in determining surgical procedure, and is considered unreliable by some of the recent writers on the subject (Goff (6)). However, it is probably true that some definite law determines the benignancy or malignancy of all tumors, and it may be that eventually histological criteria will be found on which a differentiation of the benign from the malignant chorioma can be made.

The elements which may enter into the formation of the chorioma are the cells of the two ectodermal layers of the chorionic villus, namely Langhans' cells and syncytium. Of these the Langhans' cells seem to be the element which has the power of destructive invasion and metastasis, while the syncytium apparently plays the rôle merely of an accomplice. Not all choriomas contain both elements, but they all contain syncytium. Some of those which contain both elements are benign in their course, some are malignant; but all of those containing only syncytium are apparently benign.

The syncytium as it occurs in the tumors is often not a typical syncytium, but takes the form of large cells of various shapes, with deeply staining acidophilic cytoplasm and a single nucleus varying in size, shape, and staining property. Occasionally one cell contains two or three nuclei. That these cells are really derived from the syncytium is evident from their similarity to the true syncytial masses which are often present in the same tumor. The extraordinary thing about these cells is their apparent power of wandering from their original site through the tissue of the uterus, especially into the myometrium, where they are found singly or in groups between muscle cells, in the connective tissue, and especially in relation to blood-vessels. Often they bulge even into the lumen of a vessel, and it is probably their special tendency to do this that leads to the frequent metastasis of the tumor by way of the blood-stream.

One of the striking facts connected with the benign choriomas is the frequency with which acute infection of the uterus accompanies the condition, often leading to a terminal septicemia or peritonitis. This feature is so common that some writers have called the condition "syncytial endometritis." The persistence in the recently pregnant uterus of soft, vascular, partly disintegrating tissue seems to provide an exceptional culture medium for bacteria which are accidentally present. The uterine wall, due to the presence of the tumor, remains abnormally vascular, absorption from the mucous surface is great, and the way is open for the formation of septic thrombi in the uterine veins or for the extension of the infection to the peritoneal surface.

The following case is reported to illustrate the septic termination which may occur in the presence of an insignificant and apparently regressing chorioma of the syncytial type.

History. A female Chinese, aged thirty-five, was admitted to the Sleeper Davis Memorial Hospital, Peking, complaining of palpitation of the heart and weakness. Family and past history were irrelevant. She had been married at eighteen years of age and had had six children, the last one born three and one-half years ago. One year before admission she had a miscarriage, at which time she had a severe

uterine hemorrhage, which recurred frequently thereafter until the date of admission. Physical examination showed a poorly nourished and very anemic woman, with pulsating jugular veins, a systolic heart murmur heard over the precordium and over the left chest posteriorly, and a few moist râles at the bases of the lungs. Abdominal and vaginal examinations were negative.

While confined to bed in the hospital uterine hemorrhage recurred without apparent cause. Temperature varied between normal and 100.8° F. for the first three weeks in the hospital. At the end of this time there was only a scant pink vaginal discharge. She then had a sudden rise of temperature to 104° F., after which her illness took on a septic course, with temperature remaining above 101° F. Eight days after the rise in temperature she complained of abdominal distention, but had no abdominal pain. She sank rapidly and died that night. The final clinical diagnosis was septicemia.

Necropsy was performed at the Peking Union Medical College eighteen hours after death. Externally the body showed extreme pallor and considerable emaciation. There were no petechial hemorrhages in the skin or mucous membranes. The thyroid gland was diffusely enlarged (a condition very common in Peking). The abdomen was distended and tympanitic. There was a slight pink vaginal discharge. The abdominal cavity contained about 500 cc. of gray purulent fluid, and the coils of the intestines were bound together by fibrinous adhesions. Culture of the peritoneal fluid and heart's blood yielded hemolytic streptococci. The uterus was slightly enlarged, measuring 8 cm. in length by 7 cm. across the fundus, and on being opened was found to have a rather large cavity containing a little purulent fluid similar to that in the peritoneal cavity. Smears from this fluid showed pus cells and many Gram-positive cocci in pairs and short chains. A culture was not made. In the uterine mucosa there were many small hemorrhagic areas. Otherwise the endometrium was pale, but was neither swollen nor soft. The myometrium was pale, firm, and not swollen. In the right cornu of the uterine cavity, just mesial to the point of entrance of the right Fallopian tube, was a flat, round, black and gray mass, 1.5 cm. in diameter, firmly attached by a broad base to the uterine mucosa, of very soft consistency, and with a gray, apparently ulcerated surface (Figure1). In the cervix were several small cysts containing clear fluid. In the uterine veins about the cervix and near the right fundus were several thrombi, apparently sterile. The lumen of both Fallopian tubes could be demonstrated grossly only in the outer third. Their fimbriated ends were red and edematous. The left ovary measured 5 by 1.5 cm., the right 4 by 1.5 cm. They were both flattened out behind the broad ligament. They each contained two small corpora lutea. The lungs were edematous and congested posteriorly, but showed no gross consolidation nor evidence of embolus. The spleen weighed 175 grams, was considerably enlarged and flabby and on section bright red and very soft. The kidneys were slightly enlarged, pale, and flabby, but otherwise grossly normal. At the hilum of the left kidney the renal vein contained a recent thrombus which completely filled it and extended into all the large branches of the vein. It did not, however, extend beyond the region of the kidney pelvis either toward the vena cava or into the left ovarian vein. The thyroid gland was enlarged and lobular and on section consisted of colloid glandular tissue and several large colloid cysts. The heart, aorta, liver, and other visceral organs were grossly

normal. The head was not opened. Microscopically the mass in the uterine cavity consisted of a thickening of the stroma of the uterine mucosa with entire absence of lining epithelium or glands, but containing scattered masses of smooth muscle. There were a few large blood vessels and very many small ones, especially capillary vessels dilated into sinuses. There was considerable infiltration by lymphocytes and a few polymorphonuclear leucocytes and, near the surface, many cocci which were not decolorized by the Gram stain. Scattered through this tissue were many huge cells of all shapes with one or rarely two nuclei of varied size, shape, and density, and with deeply staining, slightly granular cytoplasm. They sometimes reached one hundred micra in the longest diameter. These cells occurred both in groups and scattered singly through the tissue (Figures 2, 3, and 4). They appeared to be easily distorted by the tissue in which they lay, conforming their shape to the requirements of the surrounding structures. Thus among the smooth muscle cells they often simulated huge cells of that type (Figure 5), and about blood vessels they shaped themselves to fit the lumen or coats of the vessel wall (Figure 6 and 7). They were especially numerous about blood-vessels, sometimes abutting directly on the vessel lumen to the apparent exclusion of the endothelial cells (Figure 8). These cells were often found close together, but were not seen to be confluent like a true syncytium. In the myometrium beneath the tumor these huge cells also occurred in a few large groups as well as scattered singly in the smooth muscle or connective tissue or about blood vessels. They were present, however, only in the more superficial portion of the myometrium directly beneath the tumor, and were not found in any other part of the uterus than that immediately adjacent to the tumor.

The myometrium was normal except for the presence of the tumor cells. Its blood-vessels contained no thrombi. Sections from the remainder of the uterus showed loss of all of the surface epithelium and of some of the uterine glands. There was considerable infiltration of the superficial tissue by leucocytes, mostly mononuclear in type. There were also many Gram-positive cocci on the surface and in the tissue just beneath the surface.

The Fallopian tubes microscopically showed nothing abnormal, each having a wide lumen near the outer end and very small lumen near the uterus. About the right tube, however, several vessels, whether veins or lymphatics it was impossible to determine, were packed with polymorphonuclear leucocytes and degenerated cellular material. This was present in sections both from near the uterus and from near the fimbriated end of the tube and may have been the avenue of extension of the acute infection from the uterus to the blood-stream and peritoneum. One small vein near the left tube contained a sterile thrombus. The other vessels were normal. The ovaries each contained several rather recent corpora albicantia, but none in the luteal stage, nor were there any lutein cysts of the type sometimes present in cases of chorioma. There were active ovarian follicles in various stages of development.

The other organs showed only the changes incidental to a long illness terminated by an acute general infection. The thrombi in the uterine and renal veins were all sterile.

The points of special interest in this case are: first, the insignificant and retrogressing appearance of the tumor; second, its location close to the entrance of

the right Fallopian tube; and third, the finding microscopically, of pus in vessels leading from this region toward the peritoneal cavity and the general circulation. Without the presence of the infection which terminated the case there is little doubt but that the tumor would have ultimately disappeared entirely. While still present, however, it was probably at least a portal of entry, through its soft necrotic surface, for the extension of the infection into the uterine wall. Without the presence of the tumor the infection of the uterine cavity might have been self-limited.

The source of the uterine infection is not clear, but, with the parturient condition of the organ prolonged by the presence of a portion of the embryo, a condition existed which, especially in an ignorant person without medical attention, invited the introduction and growth of pathogenic organisms which may have been present in the vagina.

The course of the disease in this case is the same as that which occurs in a considerable proportion of cases of syncytioma. In Schmauch's summary of 206 cases of chorioma (2) seven died of sepsis, and in all these the tumor was of the benign type. In some cases of this type as in Hammerschlag's fourth case (7) there is no definite tumor in the uterus, but the mucosa and muscularis are infiltrated by syncytial cells.

This case illustrates the importance of establishing an early diagnosis of the cause of persistent uterine bleeding after abortion or parturition. It also illustrates the necessity of removing all possible tumor tissue in the presence of a chorioma, in order to avoid an unfavorable outcome from the extension of a possible infection through the susceptible tumor tissue.

I wish to express my thanks to Dr. Emma E. Martin of the Women's Union Medical College, Peking, for permitting me to examine and report this case.

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EXPLANATION OF FIGURES

Figure 1. Uterus and adnexa, showing syncytioma in right cornu of uterine cavity. Posterior view.

Figure 2. Syncytioma. Syncytial cells in tumor near surface of uterine mucosa. × 50.

Figure 3. Syncytioma. Syncytial cells in myometrium beneath tumor. × 50.

Figure 4. Syncytioma. Another group of tumor cells in the myometrium. × 50.

Figure 5. Syncytioma. Syncytial cell conformed to the shape of surrounding smooth muscle cells. × 1000.

Figure 6. Syncytioma. Syncytial cells showing varieties of shape and of nucleus. × 250.

Figure 7. Syncytioma. Syncytial cells in the wall of an artery in the myometrium. × 250.
Figure 8. Syncytioma. Syncytial cells abutting on a blood sinus in the uterine wall. × 400.
Figure 9. Syncytioma. Detail of syncytial cell. × 1000.
Figure 10. Syncytioma. Another syncytial cell. × 1000.

Fig. 1.

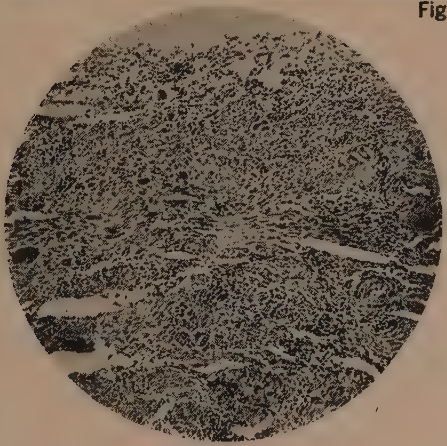
Fig. 2.

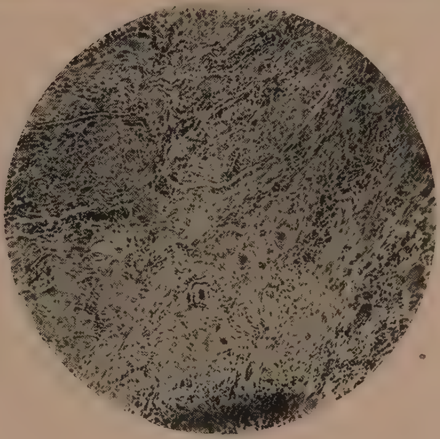
Fig. 3.

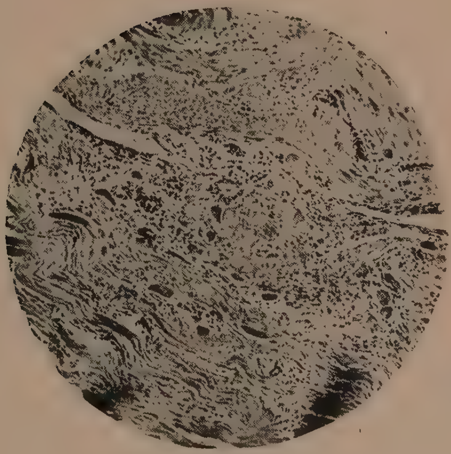
Fig. 4.

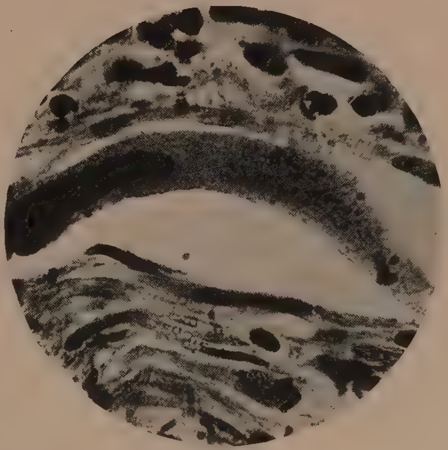
Fig. 5.

Syncytioma of the uterus (Figures 1 to 5)

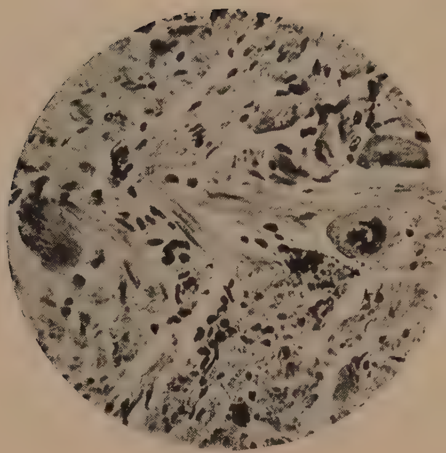

Fig. 6.

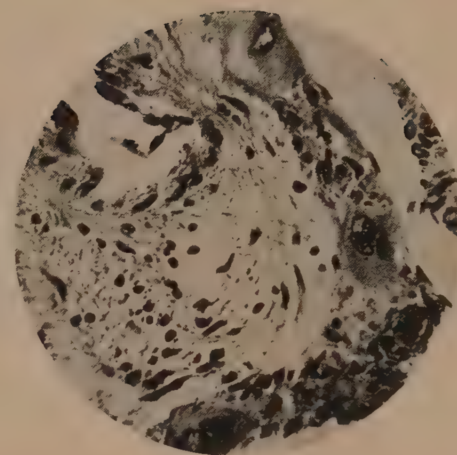

Fig. 7.

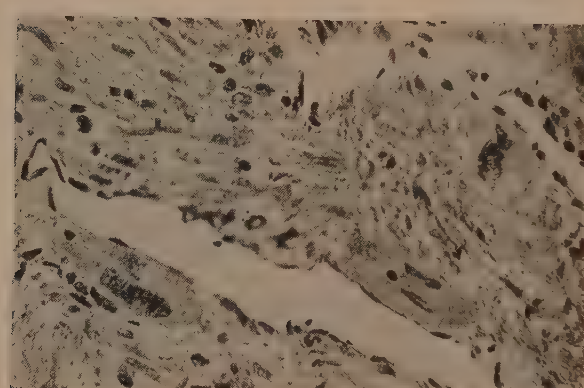

Fig. 8.

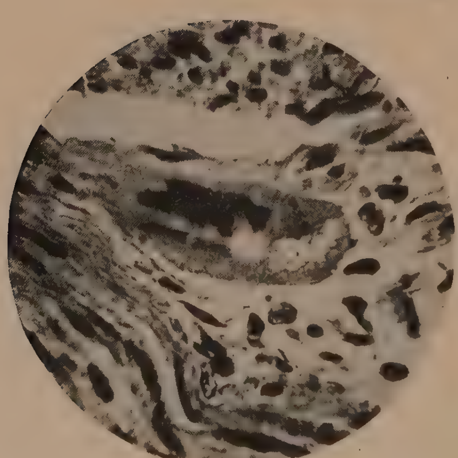

Fig. 9.

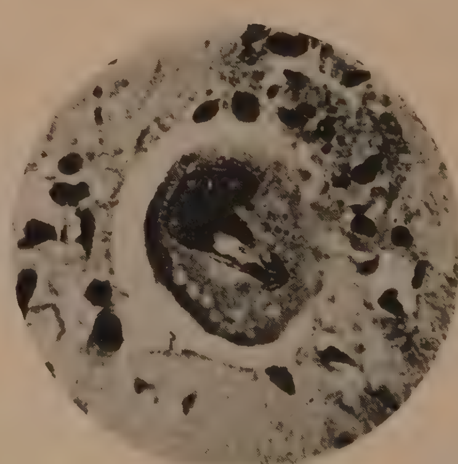

Fig. 10.

Syncytioma of the uterus (Figures 6 to 10)

TETANUS

PARTICIPANTS:

DR. ADRIAN S. TAYLOR
DR. GEORGE Y. CHAR
DR. CARL TEN BROECK
DR. JOHANNES H. BAUER
DR. SAMUEL COCHRAN
DR. J. PRESTON MAXWELL
DR. A. W. TUCKER
DR. THÉODORE TUFFIER

DR. TAYLOR: The occasion of this meeting is the incidence of tetanus in the Hsin K'ai Lu Hospital last fall, which I will briefly recount, and then Dr. Char will exhibit a case which he has under his care.

Last fall a man came into the hospital with an old ankylosis of the hip with a chronic sinus. He was put in traction, the hip was put in plaster of Paris, and the deformity was largely overcome. He was in the hospital about a week or ten days when he developed tetanus and died, in spite of extensive antitetanic treatment immediately on the appearance of the symptoms. Over the sacrum was found a bed sore, and immediately over the wound there was a piece of felt contaminated with feces. We, of course, studied the case very intensively, and the results of that study have led to the meeting this morning. Dr. Ten Broeck will report the bacteriological findings.

There have been during the last eighteen months in the Hsin K'ai Lu Hospital at least one or two other cases of death from tetanus from bed sores. I am sorry that through some fault in the indexing of the old histories we have not been able to find the case reports, but Dr. Korns remembers very distinctly at least two deaths from tetanus in the hospital, with bed sores, presumably with fecal contamination. That is a point we want to emphasize today—the importance of fecal contamination in any wound in China. The work of Drs. Ten Broeck and Bauer will be along the lines of tetanus spores in the feces of Chinese.

I will briefly recite the history of the boy who will be shown this morning. On the 27th of last April he fell from a height of about eight feet, striking upon his abdomen on a corner of a stove. He was brought into the hospital sixty-two hours later. At that time the abdomen was slightly distended, rigid, liver dullness was obliterated, and all the signs of a general peritonitis were present. Dr. Char operated immediately. He made a right rectus incision and found a ruptured intestine with fecal contamination of the peritoneal cavity. He did an enterostomy, with drainage of the peritoneum, and the boy recovered promptly. About the tenth day after operation he was found to have a stiff neck and stiff jaws. He was treated immediately with antitetanic serum, intraspinally, intravenously, intraperitoneally, and intramuscularly. We put a large amount of serum into the peritoneum, because we felt that was the source of the infection, and we put it into the muscles around the abdominal wound, for we felt that possibly the tetanus infection had gone in through the wound. The boy recovered.

Dr. Char: I reopened the wound about eight days after the first operation. The abdomen was so distended that it looked like a dilatation of the stomach. The lower abdomen was also distended, so that I thought it might be a case of temporary obstruction, and I reopened at the site of the rupture, so as to make a fecal fistula at the same time. I let the fistula go on until about June 28. Then I closed it and it healed.

Dr. Taylor: Dr. Char did not mention that he did a tangential enterostomy. He simply sutured the edges together and closed the wound.

Our part in this meeting is very small. We simply furnish the text for Dr. Ten Broeck. The feces of this boy were examined immediately, with positive results and four months later they still contained tetanus spores.

Dr. Ten Broeck: I might say just a word about the bacteriology of these two cases. In the first case we were looking for the source of the infection. At first it seemed probable that it came from the felt; a great many cultures were made by Dr. Willner from the felt, and tetanus bacilli were not found. The bed sore, or at least the borders of the sore, were excised after the patient died, cultured, and tetanus bacilli were not found. The felt contaminated with feces, however, did contain tetanus spores, and it may be that if we had examined the base of the bed sore we might have found tetanus bacilli there. The results are not as clear as we should like to have them, for we did not get the organisms from the place where they were producing toxin. We got them only from the contaminated felt. In the second case we found the organisms in the feces soon after the boy came into the hospital, and also four months later.

The first case made us wonder how commonly the gastro-intestinal tract of man contains tetanus bacilli. Going over the literature we found very few reports of positive findings. It is well known that earth, particularly street and garden soil, contains tetanus spores. It is also well known that the tetanus bacillus is probably a normal inhabitant of the gastro-intestinal tract of certain animals. In the cow the percentage is about 50; in other animals the percentage is lower. Park of New York says that in that city 20 per cent of the horses show tetanus spores in their feces.

We have been able to find only two reports of tetanus spores in the feces of man. Pazzini, an Italian, some time before 1898, examined a number of Italian peasants. In the literature available to us the number of individuals examined is not given but he found that 5 per cent of these individuals showed tetanus spores. He also found that if he grouped his cases into those that had to do with horses, 30 per cent showed tetanus spores, whereas only 2.2 per cent of the others showed the spores. Tulloch of England has quite recently reported a very interesting study, which came to our attention after we had started our work. He examined the feces of overseas troops, soldiers recently returned from France, and found that 33 per cent showed tetanus spores in their feces; whereas only 16 per cent of the civilians examined in England showed the spores. Of course these overseas men were living quite close to nature, as do so many of the Chinese. These are the only instances we have been able to discover of the finding of tetanus spores in human feces. There have been a great many investigations of the anaerobic flora of the gastro-intestinal tract of man, and I am sure that if tetanus were at all common in the gastro-intestinal tract of man at home we should have more reports of it.

Dr. Bauer and I decided to examine the stools of Chinese for tetanus spores and requested that stools of patients recently admitted to the hospital be sent to us. A brief description of our method follows. A piece of feces the size of a pea is suspended in sterile salt solution and heated for thirty minutes at 80° C. to destroy the non-spore-bearing organisms. From this heated suspension a transfer was made to a Smith fermentation tube containing bouillon and sterile rabbit kidney. After four days' incubation films are made from the sediment in the fermentation tube and examined. If the organisms characteristic of tetanus are found they are obtained in pure form from the bouillon cultures in which they predominate by repeated transfers and anaerobic platings. Those of you who are at all familiar with anaerobic work will realize what a task this has been, and I think that Dr. Bauer deserves a great deal of credit for his persistence and his success in getting the cultures pure. After we obtain the organisms pure they are grown for ten days in fermentation tubes containing bouillon and tissue. The culture is then centrifuged and the supernatant fluid in a dilution of 1 to 1,000 is injected subcutaneously into each of two mice. At the same time two mice are injected with a mixture of 100 times this amount of culture (0.1 cc.) and approximately 1 unit of tetanus antitoxin. We do not call a culture tetanus unless it has the characteristic morphology and produces a paralysis in the mice receiving the culture alone while those receiving 0.1 cc. of culture plus tetanus antitoxin show no symptoms.

We have examined the stools of seventy-two individuals and from twenty-four of these have isolated organisms which by the tests indicated above correspond to tetanus bacilli. In other words 33 per cent of the individuals examined showed tetanus spores in their feces. These figures are probably low, for we made only one examination of the stool of each person and at this time only a small portion of the feces was cultured.

The examination of the charts of these patients shows us nothing of great interest. They were, with the exception of one foreigner, male Chinese with a variety of occupations and a variety of diseases.

The question comes to one's mind, why is not tetanus more common if there is this great infection of the gastro-intestinal tract? Why do we not get it in tuberculous ulcer of the colon or amœbic and bacillary dysentery? Why is it not more common in surgical cases? There is one explanation that may account for the comparatively few cases, and that is that carriers of tetanus bacilli may have antitoxins in their blood. Examinations in Germany have shown that tetanus antitoxin is not present in human blood, but Römer has found that the cattle showing tetanus bacilli in their gastro-intestinal tracts showed small amounts of tetanus antitoxin in their blood. It is possible that we have the same thing in man, and we expect to study this in the near future. I think you surgeons might consider the advisability of giving tetanus antitoxin in cases where there is possibility of infection from feces, that is, where there are bed sores that may become contaminated, and in cases where you are going to do an intestinal anastomosis.

There are two questions you might ask: one is, do foreigners show tetanus spores in their feces? We have examined the feces of only one foreigner, and he showed tetanus spores. The other question is, why do these people not develop tetanus if they have tetanus bacilli in their feces? It has been shown a number of

times that tetanus toxin introduced by way of the stomach or rectum into the gastro-intestinal tract will not produce the symptoms of tetanus.

Another question, and an important one, is whether tetanus bacilli multiply in the intestinal tract or simply pass through. I think most people incline to the view that the existence of tetanus bacilli in the gastro-intestinal tract is a purely accidental thing, this is, that the bacilli pass through without multiplying. We tried to get some light on this question by two ways of approach. One method was to examine the feces of patients who had been in the hospital for some length of time. We felt that the food in this hospital was practically free from tetanus spores, and asked that stools be sent us from patients who had been in the hospital for a month or more. We received in all eleven stools. Three of these patients had been in the hospital between twenty and thirty days, and one showed tetanus spores. Eight patients had been in from thirty to fifty-nine days, and five of these showed tetanus spores in their stools. So that six of these eleven stools, or 54 per cent, showed tetanus spores in their stools. Of course this is a small series, only eleven cases, but the high percentage is rather startling. We have one patient who has now been in the hospital eighty-six days, who showed great numbers of tetanus spores in his stools. I went into the data in regard to the food of these patients very thoroughly, and it seems to me that contamination of their food was practically impossible. The rice they were given, which is their principal article of diet, and which might be contaminated, had been cooked under a steam pressure of 50 pounds. It is not the policy of the hospital to use this high temparature but at present the steam reducing valves have not yet been received. Their bread also had been cooked under high steam pressure. The vegetables were washed immediately when brought into the kitchen, peeled, and then cooked for varying lengths of time — ten or twenty minutes.

In one instance we have tried to estimate the number of tetanus spores per gram of feces as follows. We made a suspension of the stool, 1 gram to 10 cc. of salt solution, and heated it sufficiently to kill the non-spore-bearing organisms. From this heated suspension various dilutions were made and cultured, and we found that the highest dilution in which we could find the tetanus bacilli and from which we isolated the organism was 1 to 10,000. In other words, this patient showed 10,000 spores per gram of feces — a tremendous number. I think the only conclusion we can draw from these observations is that there must be a multiplication of tetanus bacilli in the digestive tract of man. It is not possible to take in so large a number of spores in the food given here in the hospital.

To sum up, we can say that at least 33 per cent of the Chinese show tetanus spores in their stools and that tetanus bacilli probably multiply in the gastro-intestinal tract of man. I think it would be interesting to hear from some of you who are doing surgery here in China, as to how much tetanus you encounter which might be due to fecal infection.

Dr. Cochran: This is a very interesting subject. I happen to come from a district where tetanus is excessively common — not so much in ordinary accidental or surgical wounds as in babies. I presume our soil is as thoroughly impregnated with tetanus germs as the soil of modern France was found to be. The ordinary technique of child delivery in our part of the country is somewhat crude. The usual method is to tie off the cord with a piece of ordinary string, and then to

pierce the stump with two pieces of kaoliang stalk, which comes in presumably from the cow house, and which is probably the source of infection. I have known at least two instances where seven children in succession in a single family died ten days after birth. The eighth child lived because of sterile dressings. The question of infection from the feces gives me much concern. I had a case of strangulated hernia in the hospital; I operated, and found the gut almost, but not quite dead. It was in such bad condition that I was doubtful whether or not I should do an enterostomy. I finally decided to resect it, and the gut did survive. The sac, however, was full of a turbid, ill-smelling fluid. About twenty days after the operation the patient developed a very mild attack of tetanus. We treated him in the usual way and he pulled through. Of course we were not in a position to make thorough bacterial examinations of the dressings and sutures, but as we had no other cases of tetanus from the same lot of dressings and sutures it is a reasonable supposition that they did not contain tetanus spores. I have wondered if there have been any similar cases.

As Dr. Ten Broeck has said, it is an extremely interesting question why, with so large an amount of tetanus spores in the stools of the Chinese patients, we do not get more frequent infection. As a matter of fact, we have seen cases in which the wounds were soiled with feces, but with the single exception I have spoken of we have had no case of tetanus develop in the hospital. We have had tetanus from other sources, for instance, from the dressing of a compound fracture. I should like very much to hear from Dr. Ten Broeck whether he thinks there is any possibility of spores going through the intestinal wall.

Dr. Ten Broeck: I suppose that if the wall is necrotic, or more or less necrotic, there might be a passage through it. I do not know of any work done on that question. I might say that a number of cases have been reported of tetanus in typhoid fever.

Question: Can you say whether the tetanus bacilli sometimes lie dormant in the tissues, perhaps after the manner of the typhoid bacillus, and after the patient has quite recovered, some other injury may free the organism? I have had two cases. One patient received an injury of the finger, which healed perfectly but left a slight deformity. The finger was operated upon, and very shortly afterward the patient developed tetanus and died. The other patient was a boy whose hand had been crushed and some of the fingers taken off. He was brought into our hospital at Tsinanfu several days after the accident. His general condition was good. He was kept for a few days in the ward, the wound cleaned up, and a plastic operation was done. He developed tetanus; we gave him antitetanus serum and he recovered.

Dr. Ten Broeck: It has been shown that the tetanus bacillus does lie dormant in the tissues. In fact there was so much tetanus following second operations during the war that orders were issued by the United States government and the English government that all cases that were to be reoperated upon should receive antitoxin.

Dr. Maxwell: We had quite a number of cases during the war where tetanus occurred in skin operations — wounds that had been healed for months. In one case the wound had been healed for over a year. All cases were supposed to have had antitetanus injections. I should like to ask whether there was confirmation

of the late findings of the tetanus bacilli by animal infections. You have said that in the feces there were no other spore-bearing bacilli. I was surprised to hear that, for in some of the wounds we saw during the war there was a multiplicity of other spore-bearing bacilli, and it was difficult to tell which were tetanus and which were not. In fact we were not very well satisfied with the diagnosis.

Dr. Ten Broeck: I think you misunderstood me. The gastro-intestinal tract is full of anaerobes. In fact the number of anaerobes probably equals the number of aerobes. We simply disregarded the others, confining our search to the tetanus bacilli. The organisms we have called tetanus have been isolated in pure cultures and have produced toxin, which is neutralized by tetanus antitoxin, the toxin producing the classical symptoms in mice.

Dr. Taylor: Several men have asked me about the treatment of tetanus. Dr. Spourgitis spoke the other day of a case in which he used magnesium salts, but I cannot say that I know anything about its use.

I understand that Dr. Spourgitis is using the magnesium chloride for its hypertonic action on the wound. Meltzer has published a paper on sulphate of magnesium in tetanus, but it is too dangerous to use. Generally of course you can counteract the effects by calcium chloride given immediately, but you have too narrow a margin of safety — you may not give your calcium chloride quickly enough. I never use it.

Question: I should like to ask if any of you have used carbolic acid. I have used it on several occasions, and have never seen any bad effects from it, and certainly some cases improved. Whether they would have improved in any case I cannot say. But I always try it when I have no serum. I think a point to remember is that you must give the carbolic acid until the urine becomes smoky.

Dr. Taylor: The treatment with serum is a pretty serious proposition. Colonel Gray brought a patient into the hospital a few days ago following a gun-shot wound. He had already given the man $90 worth of serum, without great benefit. We contributed 25,000 units. We hoped to have you see the patient this morning, but he died yesterday. The boy who is shown this morning received 67,000 units.

Question: Subcutaneously or intraspinally?

Dr. Taylor: Intraspinally, intramuscularly, intraperitoneally, and intravenously. I think it is very important to know the incubation period of tetanus. The length of the incubation period varies inversely with the severity of the disease.

Visitor: May I ask about carbolic acid. Was tetanus antitoxin used?

Answer: Tetanus antitoxin was used.

Visitor: I remember a case which was treated with carbolic acid and tetanus antitoxin. This case came to my knowledge in hospital practice in Chicago. A man employed in the stockyards fell and cut his nose, and two days later he developed tetanus and died.

Dr. Taylor: I remember a case of delayed tetanus in Baltimore which interested me — a patient with an osteomyelitis of the metacarpal bone of the first toe, who, sixty days after his discharge, developed tetanus, although antitoxin was given on the first admission. This patient recovered.

Question: May I mention one thing that I think the war has brought out? It seems to me that after what we have heard this morning about the prevalence

of tetanus in China it would be well to follow the lead of the armies in France with regard to prophylactic injections, and proceed on the supposition that it is our duty as practitioners here in China to give these prophylactic injections. I am interested in what has been said in regard to carbolic acid in tetanus. I come from a district where tetanus is very common. We have tried giving carbolic injections to infants — I should say we have given it to hundreds — and not one has recovered. But we gave carbolic acid injections to an adult patient in our wards who had tetanus, as there happened to be no antitoxin at hand, and that patient recovered, with, however, a paraplegia. I should like to know whether this is a common sequela of tetanus.

Question: I should like to ask a question in regard to the dosage of the antitoxin, because the second dose has very much less effect than the first, and if it should ever become necessary to give the same patient serum it would have much less power. Some people with diphtheria, for instance, prefer not to take the immunizing antitoxin, because of the danger of sensitization.

Dr. Tucker: In about two to three thousand accident cases a year we have one or two cases of tetanus. Most of those are street accidents. We think the incidence therefore is very low.

Question: Is it true that donkey serum can be used? Following a previous disease where horse serum had been used would it be a safeguard to use another serum?

Dr. Ten Broeck: I do not know whether donkey serum would be safe or not. Of course the donkey is quite closely related to the horse. The horse, is of course, the animal commonly used. If you give your patients tetanus antitoxin tell them they have had horse serum, and make them realize the importance of this, so that if they are subsequently treated with serum they can tell their next physician that they have had horse serum, and he can test their sensitivity and if necessary desensitize them. Now that so much serum is being given, it would be wise to desensitize all patients before giving serum.

A member of the Conference, made the following report concerning the work of Dr. Roberts, pathologist in the Mayo Clinic:

Even if you do not get an anaphylactic action when you give a second dose it takes about six or seven times the same amount of serum to produce the same immunity. Even when you do not get the anaphylactic action, you get the antitoxin thrown off much more rapidly. So that I suppose if the second dose were a different animal serum you would avoid the rapid throwing off.

Dr. Ten Broeck: I think that if we ever develop serum work here we shall have to use an animal other than the horse, as practically all the horses here are infected with glanders.

Dr. Tuffier: For preventive treatment of the wound I think that serum is the best thing. In the beginning of the war when we did not yet have sufficient serum we had many bad results, but when we had plenty of serum we did not have bad results, so I am sure that serum is a very good thing. Somebody has said that you have good results because you treat the wound immediately and not because you inject the serum — because you wash the wound and sterilize it. At the last meeting of the Surgical Congress the preventive serum treatment was discussed. It was never the same, for no two countries have the same technique.

QUESTION: I should like to ask two questions. First, do you notice any effect on the occurrence of tetanus as the result of the substitution of human effort for animal effort in transportation; and further, whether you have had any experience in treating tetanus by any other measure. I should like to know particularly about phenol treatment.

QUESTION: I should like to ask the question whether you have had cases of tetanus after dog bites, or things of that kind — donkey bites, horse bites, dog bites. Some cases I believe have followed the bites of dogs. We have had cases of hydrophobia, but, on the other hand, the symptoms of hydrophobia are really difficult to differentiate from those of tetanus.

DR. TEN BROECK: The phenol treatment has been discussed. I do not think, however, that any conclusions have been drawn. The cases have been comparatively few. Some of the patients recovered and some died. I do not know that anyone here would recommend it. I do not quite understand the question in regard to the substitution of human for animal means of transportation. Do you mean would there be more tetanus or less tetanus with human means?

ANSWER: I think there would be less tetanus.

DR. TEN BROECK: I think there is a great deal of tetanus here. The work reported earlier was that at least 33 per cent of the Chinese carry tetanus spores in their gastro-intestinal tract, and we know that the gastro-intestinal tract of man is much like the gastro-intestinal tract of animals.

ANSWER: Where I am living there is a large substitution of human labor for animal labor. In South China almost all the work is performed by human labor, and draft animals, except the water buffalo, are not common. Tetanus is very rare. A great deal of the work of pumping water and turning mills is performed by the water buffalo, and yet tetanus is very rare and I have been wondering whether the water buffalo is as commonly affected as the cow and the horse. I should like to mention one thing, and that is that the soil where there are sheep has been found to be contaminated with tetanus bacilli, and yet we have very little tetanus. I have not had more than fifteen cases in fifteen years.

QUESTION: This series was done here in Peking and had nothing to do with the water buffalo?

DR. TEN BROECK: Yes, it was done here, and in other parts of China the results might be very different. I do not know anything about the gastro-intestinal tract of the water buffalo. It is quite possible that districts do vary.

Service Court and Pathology Building

A Reading-Room in the Library

PATHOLOGICAL PROBLEMS IN THE ORIENT

By

William H. Welch, M. D.

I regret that a meeting of the Trustees made it impracticable for me to take the place assigned on the printed program, and I appreciate the rearrangement which has given me this opportunity to speak at one of the conferences of the Pathological Department.

I shall take the liberty of making the subject assigned to me by Dr. Mills — Pathological Problems in the Orient — somewhat incidental to certain general considerations concerning the organization and development of a modern department of pathology in China, particularly under the conditions to be found or to be created here in Peking.

A few words by way of definition may not be out of place, obvious as they may be. Pathology in its broadest and strictly etymological sense is the science of disease and includes all of medicine except the art or the purely practical side, which aims to become the application of this science. A favorite text-book of pathology in its day, that of my old teacher, Professor Wagner of Leipzig, treated the subject in this comprehensive manner, including not only general pathological anatomy and pathological physiology, but also general diagnosis, general prognosis, and general therapeutics.

Less, however, from logical considerations than from practical, didactic necessity the term pathology has been more narrowly delimited so as to include on the one hand the morphological study of disease — gross and microscopic pathological anatomy — and on the other the study of diseased function or pathological physiology, especially from the experimental side. Etiological, especially bacteriological, chemical, and physical studies are important for both the morphological and the physiological sides of pathology.

Virchow long ago — and here may I in passing call your attention to the great interest of his articles on this subject in the early volumes of his *Archiv* — pointed out that pathological physiology cannot be constructed solely from the laboratory or experimental side, important as this is, but rests upon the combination of experimental and clinical or bedside observations and studies. Thus you will not expect to find the whole of pathological physiology in such valuable text-books as Cohnheim's *General Physiology* (the appearance of which marked an epoch over forty years ago), and the more recent work of Krehl.

There was a time when the interest of the pathologist was confined mainly to morphological or anatomical studies. Coming from the school of Cohnheim I was accustomed to emphasize in former days the narrowness of this conception and the importance of experimental pathology. I have always been proud of the development of this experimental side of pathology in my laboratory by Dr. MacCallum and other assistants who followed him, and the pioneer courses in experimental pathology, which have proved to be so useful and attractive.

I always considered, however, that pathological anatomy is the central feature of a department of pathology, and the time has come when this needs to be em-

phasized. With the development of bacteriology, of pathological chemistry, and of experimental pathology, each of which has its place in a pathological laboratory, there is real danger of the neglect of pathological anatomy. Nothing could be more mistaken than the view that this has contributed all that it is capable of doing to the progress of scientific medicine, and that its pursuit has no longer the interest and significance which it once had.

I had already become somewhat apprehensive that a generation of younger pathologists was arising with little interest and little experience or training in pathological anatomy and histology, but keenly absorbed in the experimental, bacteriological, and chemical sides. The experience during the war confirmed this impression. Whereas there was no difficulty in finding bacteriologists for the laboratories attached to our camp hospitals, there was the greatest difficulty, amounting often to an impossibility, of finding in sufficient number pathologists competent to make proper autopsies, to write or dictate satisfactory protocols, to interpret the findings, and to preserve properly and work up the material obtained at autopsy.

While I am sure that Dr. Mills and his colleagues here appreciate the importance of autopsies and the cultivation of pathological anatomy in its broadest sense, you will allow me to call attention to the peculiar importance of such work here in China, where in the past autopsies have been so difficult to obtain and consequently so infrequent. Nothing is more disappointing in reading about diseases in China and in trying to form a conception of their nature than to find how unsatisfactory and meager are the pathological anatomical reports. Here there is certainly a rich field for the pathologist, so rich that one is justified in placing primary importance upon the making of autopsies and the careful study of pathological material as a function of this laboratory. It is gratifying to learn that the native prejudice against making autopsies is being gradually overcome, but doubtless much remains to be done in making the intelligent Chinese realize the essential part which pathological anatomy has played and will continue to play in the development of scientific medicine.

In this connection permit me to say a few words about the status of bacteriology in the medical curriculum. The term itself has far outgrown its original significance, including as it does frequently other microscopic parasites, and also embracing not only systematic bacteriology, but highly specialized cognate subjects like immunity. Without dwelling on these subdivisions I should like to point out that historically bacteriology, as it relates to human diseases, has developed mainly either under the ægis of hygiene or of pathology, the former shelter being more common in Germany and the latter in America, each tending to certain special lines of development. There is no question that while bacteriology will continue to be cultivated in pathological and in hygienic laboratories, this branch of knowledge has won an independent position for itself, and its progress is furthered by those who devote their entire time to its study.

While recognizing this independent status of bacteriology, I conceive that there are distinct advantages in the present arrangement in this medical college, in its inception and for some time to come, in the close alliance between the teaching and study of bacterial and other parasites and the Department of Pathology. The arrangement should be of mutual benefit. In fact I see no objection and I see

some convenience and advantage in the early development of this medical school in making pathology serve as a rather broad shelter for a number of subjects which may eventually claim their independence but which are all concerned with the laboratory study of the etiology and nature of disease and are in a logical sense divisions of pathology and may be so treated.

It is not necessary for me on this occasion to dwell upon the great interest and importance of medical zoology in its threefold divisions of protozoology, helminthology, and entomology in the study and understanding of diseases of the Orient. Nothing is more commendable than the zeal with which not a few of our medical missionaries have pursued this subject, and the success which they have attained in spite of inadequate zoological training and material handicaps. The contributions already made in so short a time by Dr. Faust, the accomplished helminthologist of this College, are an augury of the rich harvest to be gleaned in this fascinating field.

It may not be inappropriate to say a word about the task of making diagnoses for clinicians, especially surgeons, from specimens, often curettings, or other small fragments of tissue, removed for this purpose. This kind of work should be regarded as a mere incident and not allowed to become a large part of the functions of a pathological laboratory. It is often most unsatisfactory, and at the same time it is responsible work, if the decision as to treatment is made to depend upon it. I would caution the inexperienced young pathologist not to hazard in any doubtful case a positive diagnosis and especially a definite prognosis; to learn all he can about the clinical features of the case; and to acquaint himself with the correlation between pathological findings and the clinical course. There are many pitfalls which can be learned only from experience. It may here be remarked that good surgeons nowadays rarely remove fragments of tumor merely for diagnostic purposes, as the consequent risks of metastasis have become well known. The merely diagnostic work of a pathological, as contrasted with a clinical laboratory, has become relatively inconsiderable in comparison with earlier days.

I should like to say a few words, commonplace as they may seem to be, regarding the relations of teaching and of research in a medical school. It goes without saying that the primary purpose and obligation are educational. It is equally true in my judgment that research in various ways furthers this primary educational purpose. As a rule the teacher who is interested in the study of problems presented by his subject, who is endowed with the spirit of investigation, is the most inspiring teacher. Such a teacher will find his problems and will find time somehow and without neglect of the instructional side to study them. While every good medical school endeavors to fill the important chairs with teachers of this kind, those with gifts of discovery of a high order are rare, and it is not to be expected, perhaps not even to be desired, that every chair in a medical school should be so filled. Excellent service can be rendered by those whose gifts may not be conspicuous on the investigative side, who are interested mainly in teaching and the effective organization and conduct of the work of the department. The output of scientific work from a department is the greatest when many are attracted to work under a teacher who creates conditions favorable to the best kind of training and the development of the scientific spirit.

I am inclined to think that the development of independent institutes of re-

search has led some of our young men to a false perspective of the relation of teaching and research, which are historically so closely intertwined as to be inseparable in institutions of the higher learning, and it would be a pity if this historic relationship were disturbed, and I am confident that it need not be. Do not think of teaching and of research as two entirely separate and distinct functions, one of which must be sacrificed to secure the other. Recall the many examples of great teachers who have also been great investigators. It is also well for the teacher to make sure of his special aptitudes, and if these are not in the field of research he should not force himself to follow a path to which he has not the clue. He may excel in other ways which are of great service to the school.

It is hardly necessary to remind you of the peculiar importance in this school designed to train Chinese students in modern medicine, of the objective method of study as exemplified by practical work in the laboratories and in the clinics. The methods and concepts of experimental science have been until recent years entirely foreign to the traditional educational system and habits of thought of the Chinese people. In this respect China has been in the condition of Western countries before the days of Galileo, Harvey, and Newton. With this traditional background it may not be altogether easy to develop those habits of close and accurate observation under natural and experimentally controlled conditions and of just inference from reasoning based on these observations upon which the method of natural science rests, but for the future of scientific medicine in China it is of the first importance that this be done.

I hope that you will develop here a good museum of pathological specimens. That pathological department is fortunate which has attached to it someone, it may be an assistant, who is enthusiastic in the collection, preservation, and display of pathological specimens which can be made to serve an important purpose in the teaching of students.

The theme which has been assigned to me by Dr. Mills assumes that there are pathological problems peculiar to the Orient, and this is of course true. But I would remind you that these problems are not concerned solely with diseases which are peculiar to the Orient, interesting as they are. It is scarcely less interesting to study the influence of climate, of race, of housing, of cultivation of the soil, of food, of habits of living and working, and of other factors which might be specified, upon the occurrence and characters of diseases common to the Orient and other parts of the world. Much of this line of pathological and clinical study falls within what may be called comparative epidemiology or endemiology, and I conceive it to be a fruitful and fascinating field of investigation.

Take such an excellent book as Jeffries and Maxwell's *Diseases of China*. On almost every page you will find some open problem. Why is kala azar almost confined to the natives, and sprue to the foreign population? I think that you have already found here that the statements in this book regarding the occurrence of typhoid fever in China need correction. There are impressions about infant mortality, but how little is accurately known! Modern ideas regarding the development and the varieties of tuberculosis, modes of infection, the relation to what Colonel Bushnell calls tuberculization of the population and to infection in early life, the question of human and bovine tubercle bacilli, these and other questions relating to this ever interesting disease are clamoring for solution in this country. Here I

might reinforce what I have already emphasized about the importance of pathological anatomical studies. It is such studies that have the last word to say on the vexed question of the relative importance and frequency of alimentary versus respiratory infections, as may be illustrated by Opie's original and highly significant investigations of pulmonary tuberculosis. The universal use of human excrement as a fertilizer creates a number of highly important problems in hygiene and in pathology relating to hookworm and other intestinal parasites, typhoid fever and other diseases. How much is still to be learned concerning the various diseases caused by trematodes! The distribution of these diseases, which seems quite remarkable, the life histories of some of the flukes, and the pathological characters of these diseases are fascinating subjects of study. Malaria, amœbic and bacillary dysenteries, typhus, cholera, and plague are public health problems of great importance in many parts of China. There is still a mystery concerning some of the cases of splenomegaly, which do not seem to fall within any of the recognized categories. But I need not go on to enumerate problems with which you are more familiar than I am.

I have tried merely to indicate that there is a wealth of interesting pathological problems of great local significance. Here is really the romance of medicine and you are to be envied the opportunities of attacking so many interesting and important open problems. I would urge that in teaching and in investigating you keep before you these local problems, and do not settle down to just the same lines of work which you could pursue as well in Boston, New York, or Baltimore as in Peking.

Your highest ambition should be to train Chinese students in modern, scientific medicine. Some of these will be practitioners, some teachers, and some investigators, who will themselves contribute to the solution of such problems of their country as I have indicated, who will spread in their country the knowledge and the practice of the best that medicine can offer for the prevention and treatment of disease, and who will create new centers for education, investigation, and the care of the sick and injured. The consciousness that you are furthering this high purpose and thereby the health and prosperity of this great country, indeed of the civilization of the world, must be your supreme reward, and a very satisfying and enduring reward it seems to me to be.

DEPARTMENT OF OPHTHALMOLOGY

OPERATIVE CLINIC

By

Harvey J. Howard, M. D.

CASE I. EXTRACTION OF CATARACT

Hospital No. 718. A female Chinese, aged sixty-five. Vision began to diminish in right eye about two years ago; and in the left eye, a few months ago.

Ocular Examination.

Vision: O. D. Hand movements. No correction helps.
O. S. –2.00 sph. = 6/60.

Projection sense of both eyes, good.

Ophthalmoscopic Examination. This showed an opaque lens and therefore no fundus reflex visible in right eye, and marked lenticular opacities in the left lens.

Laboratory Examination. Urine and feces, normal. Wasserman, negative.

Diagnosis. Mature senile cataract of the right eye, and incipient cortical cataract of the left.

Operation. The so-called Smith-Indian operation is a method of intracapsular extraction of a cataractous lens. Colonel Smith, formerly of Amritsar, India, had a unique opportunity to develop a special technique because of the great number of his cataract cases, totaling about forty thousand in his term of about twenty-five years in India. Smith did not use a special forceps with which to pull the lens out, but applied pressure to the anterior segment of the eye by the use of a hook and a spatula to secure the expulsion of the lens. By virtue of an unparalleled experience and by the help of a marvelously clever Indian assistant, Smith proved to be eminently successful. Others who have tried his method have not been so successful.

The advantage of extracting the lens with its capsule has, however, been quite universally recognized. Therefore other safer methods have been suggested and adopted. Kalt of Germany, Knapp and Verhoeff of America have used with success special forceps for grasping the lens capsule and pulling out the lens.

An additional safeguard is the introduction before the operation is begun of a sclero-conjunctival suture, which is so inserted that it may be looped away from the field of operation, but may be pulled tight and tied, closing the lips of the wound at the end of the operation. There is a great tendency for many of the Chinese to squeeze at an inopportune moment during the operation. There are also cases who either refuse or are unable to remain quiet following a lens extraction. In such cases the use of the stitch may save the eye. In one of our recent cases, a woman, the eyes were forcibly opened underneath the bandage after the patient awakened suddenly from a nap. Only the suture saved the eye from complete expulsion of the vitreous through the wound. In her case nothing untoward happened and all progressed well following a reapplication of a dressing and a bandage.

Generally speaking the anterior capsule of a mature cataractous lens, which is a swollen lens with a comparatively tight capsule, is difficult to grasp with smooth-

bladed forceps such as Verhoeff's or Kalt's. A sclerosed lens is also difficult or in fact impossible to remove by this method. The easiest lenses to remove are immature cataractous lenses and Morgagnian cataracts.

It was decided in this case to try to extract the cataractous lens in its capsule by the use of Verhoeff's extraction forceps. Failing this, it would be a simple matter to cut through or to remove a piece of the anterior capsule of the lens, and then extract the lens in the ordinary way.

The right eye was properly prepared and cocainized for the operation. The first step in the operation was the insertion of the sclero-conjunctival suture after Verhoeff's method. The section was then made with a Graefe knife, and following this an iridectomy was done. The blades of Verhoeff's forceps were then inserted through the wound and three attempts were made to grasp the anterior capsule of the lens. This proved to be too resistant, so the forceps' blades were removed and Weeks' sharp-toothed forceps were used to tear off a segment of the anterior capsule. This released the swollen lens matter and the nucleus, which, with the aid of a lens spoon and a spatula, was successfully removed. The pillars of the iris coloboma were replaced by the spatula; the ends of the suture were drawn up and gently tied. There was no loss of vitreous and no other complications during or following the operation.

Since the lens was not removed in capsule, the posterior lens capsule remained behind. This will become fibrous and will probably require a discission later on in order to produce a clear pupillary space.

CASE 2. DISCISSION OF SECONDARY CATARACT

Hospital No. 544. A male Chinese, aged ten. Vision began to diminish in both eyes about five years ago. This blurring steadily increased until the child was practically blind. He was first seen on August 22, 1921.

Ocular Examination.

Vision: O. D. Hand movements.
O. S. Hand movements.

Projection sense was good.

Ophthalmoscopic Examination. This showed both lenses to be opaque.

Diagnosis. Juvenile cataract of both eyes.

Operation. August 25, 1921. A combined extraction with insertion of sclero-conjunctival suture was performed on the right eye under chloroform with no complications.

September 5, 1921. A linear extraction of the left lens was done under chloroform with no complications.

Diagnosis. Secondary cataract of right eye.

Operation. Discission of the secondary cataract was performed under chloroform. A good-sized elliptical pupil was made in the membrane, using Ziegler's knife needle. No complications.

Discussion. The cause of the cataract in this child is unknown. It is not a case of congenital cataract, because the loss of vision did not commence until the child was five years old. We therefore call it a juvenile cataract in contradistinction to a senile or a pre-senile cataract.

Cataracts in children very quickly become soft, because the lenticular fibers

have not yet become sclerosed and consequently their degeneration is the more rapid. In the right eye a combined extraction was performed in the hope of removing the soft lens matter in its capsule; but the anterior capsule ruptured, releasing only a very small amount of straw-colored fluid, the entire contents of the capsule. It was not possible with the child under a general anesthetic to remove the capsule then without endangering loss of vitreous; so the eye was closed and the wound allowed to heal, with the idea that subsequently an incision through the capsule could be done with safety.

With the experience of the right eye before us at the first operation, a simple linear extraction of the soft lens matter in the left eye was done.

PRESENTATION OF CASES

PARTICIPANTS:

DR. T. M. LI

DR. HARVEY J. HOWARD

DR. W. S. THACKER-NEVILLE

DR. P. S. SOUDAKOFF

CASE I. TOXIC AMBLYOPIA

DR. LI presented a case of a toxic amblyopia, admitted to the hospital on August 18, 1921, with a history of almost complete blindness coming on about three weeks before.

History. The patient was a Chinese soldier, aged twenty-one. His body was covered with pox marks, caused by an attack of smallpox which he had had about two and a half months prior to the onset of the amblyopia. During the convalescent period of the smallpox he took several doses of Chinese medicine, — one dose a day for eight successive days. Six or eight weeks after he had taken the Chinese medicine, he took six or seven green peppers with vinegar. The next day he noticed that his vision was somewhat blurred. On that day he took several more peppers and more vinegar. Following this the patient says his vision rapidly diminished, until about eight days after the onset he could scarcely see light. On the day following the second meal of peppers and vinegar he began to have a full feeling in his head, temporal headache, buzzing, and vertigo, which lasted for twelve days. No history of nausea or vomiting.

Ocular Examination. Upon admission, August 18, the vision of each eye was reduced to light perception; his pupils were dilated and immobile. The optic discs showed distinct signs of neuritis, the arteries were small and tortuous and the veins were engorged. In the right eye there was a slight hemorrhage around the superior nasal vein.

Physical Examination. Spinal Wasserman test was negative; so were otolaryngological, dental, and X-ray examinations.

Treatment. For two weeks he was given potassium iodide, 0.3 gram three times a day. Vision improved slightly up to counting fingers with the right eye at 18 inches and with his left eye at 8 inches.

On September 3 we began the hypodermic use of strychnine nitrate, $\frac{1}{30}$ grain once a day. Vision increased up to the counting of fingers at 4 feet with the right eye and 3 feet with the left eye.

Result. The optic neuritis disappeared, but the arteries were still somewhat contracted and the veins somewhat engorged. The discs were slightly pale, but not paler than is often seen in normal cases.

CASE 2. QUININE AMBLYOPIA

DR. HOWARD reported a case of quinine amblyopia in the one-year old child of a missionary, who for a severe attack of the crescentic form of malaria had been given comparatively large doses of euquinine each day for ten days, and two doses of 0.15 novarsenobenzol, one on the third day and one on the ninth day.

The physician in charge of the case on July 25, 1921, wrote Dr. Howard that "the coma, which began on the second day, continued for one week with gradual

improvement and regaining of consciousness. As soon as consciousness returned it was observed that the child could not see. The pupils were partly dilated and did not react to light. The euquinine has been given two days of each week for six weeks. The parasites were found in the blood for two weeks. No evidence of vision has yet been noticed. The child has gained in weight and strength and learned to walk alone. Small doses of potassium iodide have been started.

"The optic head seems to be white, the vessels rather small and there are small black specks on the choroid. It is difficult to get much with the ophthalmoscope in a small child.

"I frequently see paralyses accompanying malaria, but they always clear up in a few weeks. When I see the cerebral symptoms in malaria as in this child, I give a poor prognosis."

On July 29 Dr. Howard replied as follows:

"I have come to the conclusion that you are dealing with a case of quinine amaurosis. I do not believe from your description of the case that the blindness of the baby is due to the malarial toxins producing papillitis or choked disc. In this latter case the atrophy which you see comes on late and there is also a marked tendency to hemorrhages on the disc and in the adjacent retina. In quinine amaurosis the following symptoms are quite generally found: — total blindness in the beginning, pallor of the optic discs, diminution in the size of the blood-vessels, dilated and immobile pupils. There is generally associated for the first two or three days a tinnitus and a temporary deafness. Your description, with the exception of the auditory symptoms, tallies very accurately with what I have outlined.

"Prognosis: — Of all toxic amblyopias, those due to quinine generally have the greatest restoration. This restoration is confined at first to the central vision, which gradually widens. In most cases full peripheral vision is never restored. The color of the discs may remain white for months or even years but often turns to quite the normal color. Rarely is the blindness permanent. From what you have written, I am afraid that in this particular case restoration, if it occurs at all, may be only slight. At the same time, as I have stated above, there is more hope for these quinine toxic amblyopia cases than in any other type of toxins that we are acquainted with.

"For treatment I advise the use of strychnine and digitalis. Nothing else has been found to be of value."

The physician's reply of August 16 to Dr. Howard follows:

"I wish to thank you for your letter of July 29 regarding the baby with quinine amaurosis.

"About the time I received your letter the child began to show signs of returning vision. She now apparently sees clearly in all portions of the visual field."

I mention this case because in China quinine amblyopia is not uncommon. Malaria in all forms is found quite generally throughout China, and some physicians report giving enormous doses of quinine to their severe cases. The wonder is that there is not more amblyopia in China caused by quinine.

CASE 3. CHRONIC IRITIS

Dr. Li reported a case of chronic iritis with acute exacerbations in which all examinations such as of tonsils, sinuses, teeth, and gastro-intestinal tract were

negative. Blood Wasserman was also negative. But there existed an active chronic prostatitis. The iritis ran a very stubborn course until the prostatitis was actively treated.

CASE 4. DIMINSIHED VISION AND VITREOUS OPACITIES

Dr. Howard reported a case of diminished vision and vitreous opacities in which all examinations for the location of foci of infection proved negative except the X-ray examination of the teeth. This is a type of case often seen in China, perhaps proportionately as often among foreign residents as among the natives.

DISCUSSION

Dr. Howard: In Dr. Li's interesting case of retrobulbar neuritis which is before us (Case 1), we found great difficulty in getting a history complete enough to enable us to determine the probable toxic agent producing the amblyopia.

From the history we knew it had no association with the patient's attack of smallpox, because the amblyopia came on suddenly several weeks after the attack was over. It did seem that it might have been the large doses of Chinese medicine which he took following the smallpox convalescence, but here again the patient says positively that the diminution of vision came on several weeks after he had taken it.

We were finally able to secure from him the statement about his having eaten several green peppers and some vinegar on the day preceding his eye symptoms and again on the same day. He had probably eaten green peppers and vinegar before without any ill-effects, so he considered the incident at first too commonplace to mention, until our resident physician made him refer back to each meal and tell all the things he had eaten.

The suddenness and the severity of the amblyopia which has scarcely improved since the patient's admission to the hospital, and the fundus picture which showed a slight optic neuritis at the beginning, certainly made us think of wood alcohol poisoning, especially since he had headache and vertigo associated with the amblyopia during the first few days. But ordinary vinegar will not produce amblyopia, and a search of the literature failed to find any reference to amblyopia following the ingestion of peppers in any form.

Our conclusion therefore is that the vinegar, which in China is often nothing more than diluted acetic acid, must have contained some methyl alcohol. It has been impossible to confirm our suspicions by an examination of the vinegar used, but in the complete absence of evidence of any other possible cause, it does seem as though our conclusions were correct. We have not seen in the past any toxic amblyopia cases that we could definitely attribute to methyl alcohol, but we have had cases of optic atrophy that came to the clinic long after suddenly becoming blind, and in several of them we had a strong suspicion that wood alcohol was the cause.

Dr. Thacker-Neville: While in Salonika in 1917 as a medical officer with the British Army, I saw hundreds of malarial cases; most of them were benign tertian, a few were malignant.

My usual treatment consisted of putting the patient to bed and giving him 20 grains of quinine three times a day for three days and then 10 grains three times a

day for a fortnight or longer. However, I often resorted to intramuscular injections, while a colleague of mine frequently employed intravenous injections of 7.5 grains of quinine. Among these cases only once did I see quinine amblyopia. One patient who was receiving 60 grains a day developed quinine amblyopia about the fifth or sixth day of treatment. Later, in spite of injections of galyl and an intravenous injection of 60 grains of quinine, the patient died of cerebral malaria. At the postmortem examination both spleen and brain were found to contain parasites and crescents. Thus we see that a dose that was sufficient to cause amblyopia was not sufficient to kill the parasites.

Dr. Soudakoff: Cases of toxic amblyopia, especially of methyl alcoholic origin, were frequent in Russia during the great war. Immediately after the declaration of war the sale of alcoholic drinks was strictly prohibited, excluding denatured alcohol, which could be bought for techincal purposes by license from the authorities.

Denatured alcohol is ethyl alcohol made unpalatable by the addition of certain ingredients, one of which is methyl alcohol. But even the nasty taste of this combination did not prevent heavy drunkards from taking it sometimes in great quantity. From this group there were reported many cases of methyl alcohol poisoning, some of which were fatal.

During my stay in Petrograd in 1915 I had the chance of seeing several cases of methyl alcohol amblyopia in the Petrograd Clinic for Eye Diseases. Most of these patients had taken one to three glasses of denatured alcohol a day. After one or two weeks, rarely a month, they noticed marked impairment of vision, and then reported to the Eye Clinic. We found that the acuteness of vision was generally reduced to counting fingers at two or three meters. Usually the only change in the fundus was a pallor of the disc.

The director and the chief surgeon of the above mentioned clinic, Dr. Blessig and Dr. Hermann, took a special interest in these patients and did their best to improve their vision. They tried injections of strychnine, and gave them drastics and potassium iodide, but unfortunately without any good results.

The number of cases was so great that Dr. Blessig called an extraordinary meeting of the Petrograd Ophthalmological Association, where preventive measures were discussed. All the members present stated that they had not succeeded in producing even the slightest improvement in vision.

I cannot tell exactly how many cases of amblyopia were registered in that clinic during my six months' stay there, but I am sure that at least one new case was registered every week. The average number of new out-patients amounted to 500 a month.

OPERATIVE CLINIC

COMPLETE TENOTOMY AND RESECTION IN FOUR DIFFERENT TYPES OF STRABISMUS

PARTICIPANTS:

DR. HARVEY J. HOWARD
DR. T. M. LI

CASE I

An American medical missionary, male, aged fifty-three. Complained of moderate photophobia, headache more or less constant, and an occasional diplopia. Eyes tired very readily, especially when using them for close work. Recently had a small ulcer on left cornea, which healed without serious complications.

Ocular Examination. Manifest refraction showed:

Vision O. D. +.50 sph.+ .25 cyl. ax. 150° = 6/4.5
O. S. +.25 sph.+1.00 cyl. ax. 180° = $6/6^{+3}$

There was an exophoria of 4.5° and a right hyperphoria of 10° for distance and orthophoria for near. Associated-parallel-movements' tests revealed an under action of the left eye looking up and to the left.

External examination showed a tiny centrally placed nebula on the left cornea. Ophthalmoscopy, negative.

Diagnosis. Paresis of the left superior rectus.

Operation. Complete tenotomy of the right inferior oblique was done following novocaine and adrenalin injection. An incision 12 mm. long was made through the skin of the lower lid opposite the orbital margin of the superior maxillary bone. Following the tenotomy the skin wound was sutured with three fine silk stitches.

Result. The sutures were removed on the second day following the operation. Muscle balance tests with the eyes in the primary position showed that the hyperphoria was completely corrected by the tenotomy. The lateral deviation was not appreciably affected.

CASE 2

A male Chinese medical student, aged twenty-three. Complained of headaches and frequent diplopia.

Ocular Examination.

Vision O. D. −3.00 sph.−.50 cyl. ax. 45° = $6/4.5^{-1}$
O. S. −3.25 sph.−.50 cyl. ax. 180° = $6/4.5^{-1}$

The patient was able to fuse, but only for a moment or two at a time. An examination of the muscle balance revealed an esotropia of 20° and a right hypertropia of 20° for distance and an esotropia of 9° for near. Associated-parallel-movements' tests revealed multiple motor anomalies of both eyes, chief of which were a complete underaction of the left eye and a marked overaction of the right eye in looking up and to the left.

Diagnosis. Paralysis of the left superior rectus and spasm of the right inferior oblique.

Operation. Complete tenotomy of the right inferior oblique following novacaine and adrenalin injection.

Result. Two days later muscle balance tests showed the right hypertropia of 20° reduced to a right hyperphoria of 1° only. The lateral deviation was practically the same as before the tenotomy.

DISCUSSION

These two cases of tenotomy of an inferior oblique muscle represent a type of operation which has rarely been done. In the minds of some it is a radical procedure to cut a muscle of one eye, because a muscle of the other eye is paralytic or paretic. A decision to do so must, therefore, be based upon sound reasoning to have any justification whatever.

Case 1 represented paresis of the left superior rectus producing a marked vertical deviation of the visual axes, which however was only latent, therefore fusion existed. In Case 2 there was no fusion, therefore a hypertropia which was associated with an esotropia. The strabismus was a disfiguring one.

In each case the purpose of an operation was to dimish or completely annihilate the vertical deviation. This could best be done by producing the same sort of limitation in the associated antagonist of the paralytic superior rectus; i.e., a tenotomy of the right inferior oblique in each case was the only thing to do. It is true that the ability of both eyes to look up and to the left would then be distinctly limited, but this inability would be equal in the two eyes, or practically so. One patient has already learned to compensate for the diplopia induced by turning his head rather than his eyes, so for him the result will be the removal of the constant eye strain attendant upon overcoming the high degree of hyperphoria.

CASE 3

A female Chinese student, aged seventeen, with history of scar on the right cornea and a convergent squint of the right eye that occurred following an attack of smallpox in childhood.

Ocular Examination.

Vision: O. D. Counts fingers at 2 feet. No correction helps.

O. S. $+3.25$ sph.$+.50$ cyl. ax. $90° = 6/6^{+3}$

A dense central opacity of the right cornea. No anterior synechia. Muscle balance tests were unsatisfactory, but for near sight there was at least 70° of esotropia. There were multiple motor anomalies, chief of which were a marked overaction of the right internal rectus and an underaction of the right external rectus.

Diagnosis. Right esotropia caused by amblyopia exanopsia.

Operation. For cosmetic purposes a complete tenotomy of the right internal rectus was done following local anesthesia. It was the intention to follow the tenotomy by a resection of the right external rectus, but the immediate result of the tenotomy was so nearly complete that it seemed wise to delay any further procedure until the final result of the first operation was fully established.

CASE 4

A female Chinese teacher, aged twenty, with a history of convergent squint of the left eye since babyhood.

Ocular Examination.

Vision O. D. + .25 sph.+.25 cyl. ax. 90° = $6/7.5^{-1}$
O. S. +1.00 sph. = 1/60

Esotropia for distance of 25°, and for near of 35°; no hypertropia. Associated-parallel-movements' tests showed multiple motor anomalies of both eyes, chief of which were a marked overaction of the left internal rectus and a marked underaction of the left external rectus.

Diagnosis. Left esotropia with amblyopia exanopsia.

Operation. Resection of the external rectus and complete tenotomy of the internal rectus of the left eye. It was the original intention to follow the resection of the left externus by a graduated tenotomy of the left internus, but it was found at the time of the operation that the latter procedure was insufficient, so a complete tenotomy was performed.

INTERESTING CASES OF 1920–21

PARTICIPANTS:

DR. HARVEY J. HOWARD
DR. T. M. LI
DR. HENRY E. MELENEY

CASE I. NEURO-EPITHELIOMA

A female child, about two years old, was admitted to the hospital from the eye clinic on January 24, 1921, with a large tumor mass involving the eyeball and protruding from the right orbit, and with loss of vision of the left eye.

History. The parents first noticed that the vision of the child's right eye began to diminish about five months prior to admission. The vision rapidly grew worse and finally the eye became totally blind. At this stage the pupil had a yellowish color. Two months later the eye appeared larger and protruded. Shortly after the eyeball ruptured and a tumor was then seen protruding from the ruptured globe. The tumor then grew very rapidly and the suffering of the child increased. Shortly after the tumor ruptured through the right eyeball, the parents noticed that the left eye was also losing its vision and that the pupil was becoming grayish in color.

Ocular Examination. Examination of the right eye showed a tumor protruding from the orbit for about 5 cm. anterior to the orbital margin. Both lids were quite adherent to the tumor and were markedly stretched over the base of the tumor. The growth was nodulated, beefy red in color, bled when handled, and had a very foul odor. Signs of an eyeball could not be recognized, although a knob at the anterior end of the tumor indicated the probable position of the globe prior to its disintegration.

Examination of the left eye showed it to be sightless, with a widely dilated and immobile pupil through which a dirty yellowish irregular-shaped mass was seen with the unaided eye. With an ophthalmoscope, no red reflex was visible. The mass did not move and appeared to extend forward to about 4 or 5 mm. from the lens at its temporal border and to about 2 mm. at its nasal side. The surface of the mass was somewhat nodular.

Physical Examination. Child had fairly good physical development, still being breast-fed. She appeared to be listless and in pain; was sallow and anemic looking. There were a few moist râles heard in the chest, due to the existence of a mild bronchitis.

Laboratory Examination. Urine, normal. Blood examination: white blood cells, 11,000; red blood cells, 4,976,000; hemoglobin, 35 per cent (Tallquist).

Clinical Diagnosis. Neuro-epithelioma of both eyes.

Operation. Total exenteration of the right orbit was done under ether. It was our intention to use radium as soon as the condition of the wound permitted, but the parents took the child home the following day and brought it back only twice for dressings, after which they did not return again.

Result. From a personal visit to the child's home we learned that the child died about four months after the operation. The parents said the tumor had refilled the

orbit and at the time of death protruded as far as the margin of the orbit. Death was probably due to glioma or neuro-epithelioma of the brain.

Pathological Report. Dr. Henry E. Meleney

Microscopic Examination. Sections all showed approximately the same picture. The tissue consisted almost entirely of tumor cells lying close together in a continuous mass, and held in place by a very sparse connective tissue stroma. The tumor cells were of medium size, had oval vesicular nuclei and very little demonstrable cytoplasm. No definite fibrils were visible between the cells, but in places the cells were of spindle shape and their cytoplasm reached out to a pointed end. Mitotic figures were present in small numbers. There was a tendency to necrosis of tumor cells, sometimes at a uniform distance from large blood-vessels, sometimes in little scattered areas not related to blood-vessels. In the necrotic areas some cell nuclei retained their staining property and shape. Here also was considerable brown pigment, probably from broken down red blood cells. There were no definite "rosettes," but in a few places cells were arranged radially about a central red mass containing several nuclei, not unlike a foreign body giant cell. Where the tumor had broken through the choroid of the eye a band of black pigment (melanin) was seen. The posterior sclerotic layer was also present as a hyalinized fibrous layer. One section showed the remains of an extrinsic eye muscle.

Pathological Diagnosis. Glioma of retina.

CASE 2. NEURO-EPITHELIOMA

A female child, aged fifteen months, was admitted to the hospital from the eye clinic on August 14, 1921, with a tumor protruding from the left orbit.

History. Parents first noticed when the child was three months old that its left eye could not see as well as the right. Shortly after, they observed a white spot in the pupillary space which grew larger and larger. Four months ago the child had an attack of smallpox which lasted for one month. After recovery the parents noticed a mass about the size of a small pea protruding through the left pupil into the anterior chamber. The tumor grew rapidly and finally ruptured the eyeball about two months before admission. From the time of rupture the mass grew with great rapidity, pushing the lid margins apart and protruding more and more from the orbit. On two occasions the mass was injured by falls of the child which caused profuse bleeding. The tumor has bled a little many times.

Ocular Examination. The right eye was normal in every respect. No trace of the left eyeball was visible. In place of it there was a large tumor protruding for 3.5 cm. from the margin of the orbit. Its vertical diameter was 6 cm., its horizontal diameter 6.5 cm., and its maximal circumference 22 cm. It had a dirty red color, was somewhat irregular, and at several places had broken down and exuded a bloody fluid. The odor of the mass was very foul.

Physical Examination. Child was well developed but sallow, still being breast-fed. No abnormalities except a weak and rapid heart-beat. Blood examination: white blood cells, 57,000; red blood cells, 2,592,000; hemoglobin, 45 per cent.

Three days later, because the child seemed to grow markedly weaker, 200 cc. of blood (Group 4) were transfused intravenously. The general condition of the child considerably improved after the transfusion. Two days later, blood examination

showed: white blood cells, 29,800; red blood cells, 3,768,000; hemoglobin, 65 per cent.

Clinical Diagnosis. Neuro-epithelioma.

Operation. Two days after transfusion, total exenteration of the left orbit was done under ether. There was no evidence of tumor extension beyond this orbit.

Result. For ten days the child continued to improve; it gained in weight and seemed playful and happy. Dressings were done daily. The child then developed nausea, vomiting, and high fever, grew rapidly weaker, and died in four days.

CASE 3. GLAUCOMA

Dr. Howard presented a case of absolute glaucoma of both eyes in which linen threads had been inserted for filtration and experimental purposes. Abstracts from the history follow:

The patient was a male Chinese, aged fifty-nine. Symptoms of glaucoma came on in the left eye about two years ago, and in the right eye about a year ago. Both eyes became blind about three months ago.

Upon admission on August 6, 1921, we found only the faintest perception of light in each eye. Tension taken with McLean's tonometer was O. D. 50 and O. S. 80.

Coarse linen threads were drawn through the anterior chamber close to the iris angle by means of a Graefe knife with a small hole in the blade for carrying the thread. The first procedure of the operation was to undermine the conjunctiva up to the limbus using the same method employed in a trephine operation. This was done on opposite sides of the cornea. The knife was then inserted beneath the undermined conjunctiva on one side, and into the anterior chamber, coming out with the counter-puncture beneath the undermined conjunctiva on the other side, the assistant holding the flap up in the meantime. The knife was pushed through the globe until the hole in the knife became visible, when the linen thread was put in, and then the knife was drawn back and out of the globe, pulling the thread after it. The two ends of the thread were cut within 2 mm. of their exits from the chamber. The conjunctival flaps were brought back and sutured securely so as to cover the ends of the threads.

One of the threads could readily be seen lying across the surface of the iris in the anterior chamber, but the other thread was placed too close to the periphery of the chamber to be seen. During the past six weeks the tension has been taken on an average of every second day. The tension has ranged from 27 to 60 in the right eye and from 35 to 75 in the left eye. The tension during that period has been coming down. During the past week it has averaged 30 in the right eye and 45 in the left.

DISCUSSION

Dr. Howard: The threads were not inserted for the purpose of direct filtration as is done in Zorab's operation where silk sutures are inserted. Linen sutures were used because they are completely absorbed within a few weeks after being placed in living tissue. The question to be decided was whether, following the absorption of the threads, channels lined by endothelium were left behind. I knew that Dr. William Sharpe of New York had successfully produced drainage in hydrocephelus

cases by using linen threads in the brain, and if the drainage continued after the threads became absorbed it seemed obvious that some sort of open channels must have taken their places. With this in mind, while working with Verhoeff in Boston in 1918, I inserted linen threads in the eyes of rabbits. In less than two months the threads had entirely disappeared. The rabbits' eyes were enucleated and examined microscopically. No evidence of the threads remained; nor was there any evidence of filtration channels to be found.

I felt, however, that the experiment should be tried upòn a human being if possible, and selected a case in which there was as much hope for improvement by this method as by any other. It is too early to state anything definite about the linen thread method. Certainly the tension has been materially lowered in both eyes. The tension of the right eye has been within normal limits for the past two weeks, and the tension of the left is slowly coming down. There is distinct evidence that the thread which has been visible through the cornea is being absorbed. In another month I should expect it to disappear entirely. At that time our conclusions should be more definite as to the value of the method.

OPERATIVE CLINIC

THREE CASES OF EXPRESSION FOR TRACHOMA

PARTICIPANTS:

DR. HARVEY J. HOWARD
DR. T. M. LI

CASE I

A male Chinese clerk, aged thirty.

Diagnosis. Chronic trachoma of both eyes and partial ptosis of the right upper lid.

Operation. Heisrath's resection of the tarsus of the right upper lid.

CASE 2

A male Chinese medical student, aged twenty-six. Had a chronic trachoma for years, for which he had been treated in another hospital. All signs of an active trachoma had disappeared, but the palpebral conjunctiva showed many scars and the lids many wild hairs.

Diagnosis. Trichiasis of both upper lids.

Operation. Modified Streatfield-Snellen operation was performed on both upper lids.

CASE 3

A male American child, aged five.

Diagnosis. Follicular trachoma of both eyes.

Operation. Expression of the contents of the trachomatous follicles of both eyes under ether anesthesia.

DISCUSSION

DR. HOWARD: Cases 1 and 2 are trachoma in the third or final stage. Fortunately they have escaped with the cornea of each of their eyes in fairly good condition. The scar tissue formation in the conjunctiva, however, has produced a thickened deformed tarsus and a partial ptosis in one case, and a growth of wild hairs in the margin of the upper lids of the other.

In the first case a removal of most of the tarsus through a double elliptical incision in the conjunctiva of the upper lid was done. Mattress sutures, which also held in position the lower ends of the levator muscle fibers, were put in through the lid.

In the second case a plastic operation of the upper lids was done for the purpose of deviating the course of the wild hairs. The modified Snellen operation has with us proved to be the quickest operation and one whose results are excellent.

In Case 3 the disease was still in the first stage. Therefore there was no involvement of the cornea or deformity of the lids. The problem was to eradicate the disease from the conjunctiva. In our experience we have found that an expression of the contents of the trachomatous follicles, with as little traumatism as possible, greatly hastens the cure. Following such an operation there should be daily rubbings of the diseased lids with mercuric chloride 1-500 and boric acid powder. These remedies are applied with pressure by toothpick swabs. The use of zinc sulphate in 0.25 or 0.5 per cent solution is advised several times a day. Treatment in such cases will probably have to be continued for four or five months.

PRESENTATION OF CASES

PARTICIPANTS:

DR. HARVEY J. HOWARD
DR. T. M. LI
DR. GEORGE E. DE SCHWEINITZ

CASE I. TUBERCULOUS UVEITIS OF BOTH EYES. DR. HOWARD

A male Chinese, aged seventeen, a pork-seller's assistant, was admitted to the hospital August 12, 1921, complaining of blurred vision of both eyes.

History. His family history and past history were negative. There was no history of injury. He first noticed about one month ago that his right eye was red. A few days later the vision of that eye became blurred. This blurring steadily increased. The left eye became affected in the same way five days ago and the vision steadily diminished.

Ocular Examination.

Vision O. D. Hand movements.
O. S. 6/20.

There was moderate circumcorneal infection of both eyes, but no other involvement of conjunctiva and none of the sclera. The cornea of the right eye was very hazy from a general parenchymatous keratitis; the left eye was only slightly so. On the lower posterior surface of the right cornea were a dozen or more discrete milky spots or deposits resembling mutton fat droplets, varying from 0.5 to 2 mm. in diameter. On the posterior surface of the left cornea there were numerous fine deposits which had not become discrete.

The iris of each eye was dull in color, and the pupils were slightly irregular, but there were no synechiæ. The pupils reacted to light and accommodation, but the right one only sluggishly. Tension with the McLean tonometer was O. D. 45, O. S. 28. No clear fundus reflexes could be obtained, the media of the right eye being the more cloudy.

Physical Examination. General physical examination negative. Examination of teeth and accessory sinuses was also negative.

Three diagnostic subcutaneous tuberculine tests indicated the presence of an active tuberculosis. Wasserman test proved to be positive, ++.

Treatment. During the past four weeks the patient received three doses of arsaphenamine and three therapeutic injections of old tuberculine. In addition he was given atropine instillations, and hot compresses for his eyes, and potassium iodide by mouth.

Result. The haziness of the cornea almost completely disappeared (September 22), the deposits on the posterior corneal surface changed from day to day, but tended to gather around the periphery, leaving the central area practically free.

It was possible to see that the vitreous of the right eye was filled almost completely with massive opacities. The vitreous of the left eye was quite cloudy, and contained large membranous opacities, but the details of the disc and vessels could be made out fairly well after the eye had been kept quiet for a few moments. The vision of the eye had not improved since admission.

Diagnosis. The diagnosis of the cause was the double infection of tuberculosis and syphilis. The tuberculous uveitis was probably aggravated by the general luetic infection.

CASE 2. PRIMARY OPTIC ATROPHY. DR. LI

A male Chinese, aged forty-five, complained of blindness which began to come on about a year ago. Admitted both syphilitic and gonorrheal infections twenty years ago.

Ocular Examination. Vision of both eyes was reduced to faint light perception. Pupils were semidilated, round, and did not react to light. Ophthalmoscopic examination showed that the media were clear, the disc margins regular and sharply defined, the disc surfaces had a distinct grayish pallor, and the arteries were contracted.

Physical Examination. The spinal fluid Wasserman was positive, ++++. Dental examination revealed the presence of several abscessed roots. These roots were subsequently extracted.

Diagnosis. Primary optic atrophy due to syphilis.

The presentation of these cases was followed by an informal discussion by Dr. George E. de Schweinitz of some newer aspects of uveal tract disorders and therapeutic measures for their relief.

South Residence Compound

North Residence Compound

DEPARTMENT OF OTOLARYNGOLOGY

OPERATIVE CLINIC: ESOPHAGOSCOPY

By

A. M. Dunlap, M. D.

History. Male Chinese, aged sixty-four. Complaint, difficulty in swallowing solid food. Duration, about two months. There was considerable loss in weight and strength. On three occasions there was vomiting about two minutes after eating. Had had occasional pain in region of the stomach. Was able to take liquids.

Physical Examination. Fluoroscopic examination showed incomplete constrictions of the esophagus above the level of the ninth thoracic vertebra. The outline of defect was ragged, suggesting carcinoma.

Operation. Dr. C. Jackson does most of his esophagocopies under cocaine, rarely ever using ether. In an old man such as this patient we should look for a stricture, caused by malignancy, and I suspected that was what we should find. A 12″ Mosher esophagoscope was introduced down past the esophageal opening behind the larynx. It was inserted with a mandrin until it was below the pharynx. The mandrin was then withdrawn and the tube pushed down gently, always with the end of it in view, to avoid the danger of going into fragile tissue. The Jackson esophagoscope is much smaller and much easier to insert, but in using this instrument it is much more difficult for the average individual to observe what is on the other end.

Jackson (1) makes a statement that no one should attempt to remove foreign bodies from the esophagus until he has performed the operation at least 100 times. (Dogs are generally used.) Thus far our College has not used dogs, but I think now that we are to have a laboratory we should do dog work. In the dog we meet with very much the same condition as in man, except that the larynx is straight down.

In the present case the esophagoscope was slowly introduced for its entire length. Only normal esophagus wall was demonstrated. Location of the aortic arch was demonstrated. The 12″ esophagoscope was withdrawn and a 15″ instrument was then introduced. Suction was used to clear the field of fluid. A small tumor mass was found on the posterior wall of the esophagus, which partially obstructed the lumen. Grossly this tumor appeared to be a fairly advanced malignant growth. With a biting forceps a small portion of the tumor was removed for examination. This was followed by slight bleeding.

The difference between the blocked esophagus and the normal smooth esophageal wall above the constricting tumor was demonstrated.

The esophagoscope was gently removed.

Demonstration of the use of Mosher's laryngoscope followed.

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OPERATIVE CLINIC: RADICAL MASTOIDECTOMY

By

J. Hua Liu, M. D.

History. Patient complained of purulent discharge in left ear which had lasted for twenty-five years. Had had no previous nose or throat trouble. At age of seven had had painful swelling over the left mastoid region, which suppurated after ten days. After that time there was a discharge daily from the wound, which lasted for more than a year, after which time the wound healed gradually and the discharge stopped. After the discharge had ceased from mastoid region, patient noticed a foul discharge from the ear on that side, which lasted up to time of observation. Had had headache and dizziness previously for a few days. No fever.

Physical Examination. Right ear normal. Left ear-auricle and external auditory canal in good condition. Tympanic membrane was gone and the promontory was covered with granulations, considerable discharge in the canal. Old scar was seen over upper portion of mastoid region. No mastoid tenderness.

The radical mastoid operation has for its purpose the union of the external auditory canal, the middle ear, antrum, and the mastoid wound into one cavity, capable of being drained without interference.

The radical mastoid operation was called for in this case principally for six reasons:

1. Long duration (twenty-five years).
2. Did not yield to treatment.
3. Tympanic membrane gone, with malleus and incus necrosed away.
4. Granulations on promontory.
5. Loss of hearing.
6. History of acute attack twenty years ago.

Operation. Iodine preparation of the area. The usual post auricular incision was made down to the bone, except at the uppermost portion, where it was inadvisable to cut through the temporal muscle. The periosteum was then lifted and retracted, exposing the cortex. The landmarks were then visible. Here was the bony canal which was just internal to the anterior retracted flap with the spine of Henle just below its superior margin. The latter indicated the level of the antrum. As a rule chisels and gouges are used to remove the cortex of the mastoid, although some operators use burrs. In the present case we found the mastoid was of the sclerotic type, which had no cells. I then saw a cavity which was filled with cholesteatoma communicating with the antrum. The antrum and the mastoid cavity were made as large as possible.

In clearing out the uppermost and posterior portions of the mastoid process one has to be very careful not to expose or injure the dura nor the lateral sinus. In the manipulation of the antrum, caution should be exercised to avoid injury to the antral mucosa and to the horizontal semicircular canal which lies in the floor of the antrum. The posterior canal wall was now removed by chisels. The bridge was

then removed. During manipulation in this region, the anesthetist must keep watch over the corresponding eye and lip, and must give warning of any twitching which indicates that the operator is working near the facial nerve. In view of the danger of recurrence of infection through the Eustachian tube, and the interference with healing, the latter lumen was obliterated by Yankauer's curettes.

Plastic Flaps

QUESTION: Supposing you do not make a flap?

ANSWER: The purpose of the flap is to provide a sufficiently wide opening for dressings and drainage through the external auditory meatus and to encourage the growth of an epithelial covering over the cavity. Incision is carried from within outward toward the lower conchal margin, then a round flap is cut out of the concha so that the incision ends at the canal margin. The cartilage of the concha exposed by the flap is removed and then the flaps are sutured. The cavity is loosely packed with iodoform gauze strips through the external auditory meatus and the postauricular wound sutured without drainage.

OPERATIVE CLINIC: REMOVAL OF TONSILS AND ADENOIDS

By

A. M. Dunlap, M. D.

I had planned to show the different methods used in the removal of tonsils, but as too often happens in China, the patients did not put in their appearance; but I was able to demonstrate the so-called *Boston method* as to technique of operation and position of the patient.

This position may be criticized by some as being one which is somewhat dangerous, due to the upright position. There is no doubt about the recumbent position being an ideal one if you can do just as good an operation. In the upright position you must always be sure never to have your patient so deeply under ether that his reflexes are lost. In Boston, the upright position is used because it is a normal one. Of course it has its disadvantages. When statistics were taken a few years ago, it was not felt that there was any more danger from the upright position than from the recumbent one.

When the soft palate is touched and the patient gags, you know he is not completely under. You must have relaxation if you are going to do a proper operation. Be sure you have a good tenaculum which will grip the tonsil and will hold. The tonsil is located in a sort of box,—in front, the anterior pillar formed by the palato-glossal muscle; behind, the posterior pillar formed by the palato-pharyngeal muscle; to the outer side, the broad muscle of the pharynx. This can be pushed outwards, without going through the large vessels nearby, if the tissues are healthy. In children we find a great deal of stimulation of the glands. This mucus and saliva can be bailed out as the larynx is always under control.

The patient under operation was in a condition to cough up anything entering the larynx. The method of removing the tonsils employed in this case is called the snare method. I did not want to enter the pillar. I incised the plica, that is the fold of mucous membrane which was reflected from the pillar to the tonsil.

Going through the single layer you get directly on this white glistening membrane which is the capsule of the tonsil. Get the capsule of the tonsil complete and then do not worry about the tonsil. Before removing the tonsil from the tenaculum you follow it around and see that you have the capsule intact with no breaks.

Question: Supposing there were breaks?

Answer: Go back with the tenaculum and snare. Ten years ago we used not to be very anxious about a certain amount of bleeding, but now a patient is never sent away from the operating room with any signs of bleeding.

You can see that this fossa is perfectly clear.

We rarely, if ever, make a tie. However, when a tie is made, we use silk or catgut. When necessary we use hemostats to clamp the bleeding points for a few minutes.

Successful removal of the tonsil depends upon getting good hold with the tenaculum and dissecting the capsule, without going through into the tonsil. If you watch, you will see that the end of the snare canula travels behind the tonsil thus showing what dissection is, if any, lacking. I always put the snare canula above the tonsil. You must be careful not to get your uvula into this instrument.

This patient did not have very much plica. Care was taken not to enter the pillar. I dissected down to the floor in order to free the tonsil. It was freed first from the anterior, then from the posterior pillar. This could be dissected either with a knife or scissors or dissector. The snare was inserted, screwed up, and the tonsil removed. It was perfectly clear that there was no more tonsil up there. The pillars here were intact, so that the throat contour was preserved. The muscles were intact. Both tonsil fossæ should be dry.

The adenoid was removed with an adenotome. By going behind the palate and up as far as possible what is left could be removed with the finger-nail. The patient was then bent forward so that the blood and whatever remained of the adenoids could pass out.

DEPARTMENT OF NEUROLOGY

SYPHILIS OF THE NERVOUS SYSTEM

By

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The incidence of syphilis in China seems to be about the same as in Europe and in America, and the forms thus far encountered in this hospital indicate that the clinical manifestations of the disease do not vary greatly from those seen in other parts of the world.

From the experience of various writers it is probable that 30 to 40 per cent of all necropsies would show active or healed lesions; that $\frac{1}{4}$ to $\frac{1}{2}$ of 1 per cent of general hospital patients and $1\frac{1}{2}$ per cent of neurological patients have syphilitic lesions of the nervous system; and that 8 per cent of all syphilitics have involvement of the nervous system.

Examination for syphilis and laboratory tests are advised in patients presenting the following conditions: (a) general faulty nutrition and lack of resistance in children and young adults; (b) hemiplegia or other vascular accidents in adults before middle life; (c) epilepsy starting after thirty-five; (d) headaches not otherwise explained.

PATHOLOGY

The essential lesion is an infiltration of lymphocytes and plasma cells, chiefly perivascular, with a tendency to the formation of new connective tissue and capillaries. Infiltrations are called gummata, if of sufficient size. The cause is the *Treponema pallidum* discovered by Schaudin and Hoffman in 1915. The following are the mechanisms by which malfunctioning is produced: (*a*) stoppage of arteries, veins, or lymph channels; (*b*) obstruction or irritation from adhesions; (*c*) toxic effects of the virus. Disturbances then follow according to the functions of the structures interfered with, such as: (*a*) ischemia, atrophy, edema, arteritis, aneurism, and apoplexy; (*b*) pressure upon nerves and centers, cortical irritation, hydrocephalus, and tumor symptoms; (*c*) tract degeneration and death of nerve cells.

ILLUSTRATIVE CASES

Cases from the wards of the Union Medical College Hospital were shown as examples of the following types of the disease:

A. Blocking of Peripheral Nerves by Syphilitic Infiltrations within the Nerve or in the Pia-Arachnoid around It, or Both

Case 1. Male, aged forty. Alcoholic. Syphilis contracted ten years ago. Blood and spinal fluid Wasserman tests strongly positive. Recently suffered an attack of dizziness with headache. Then upper lip became weak and within a few days the whole musculature of the facial nerves of both sides was paralyzed.

Attention was called to the infrequency of bilateral facial nerve paralysis as an isolated symptom. The condition has been observed in syphilitics.

B. Infiltrations in the Meninges, Especially of the Base of the Brain

Case 2. Male, aged about thirty. Brought into hospital a month ago in coma. No history. Blood and spinal fluid Wassermann tests strongly positive. Coma disappeared in a few days after salvarsan injection.

Examination. Incomplete Argyll-Robertson pupils; complete deafness with tinnitus; great excitabilty of all muscles to direct tap; no paralysis; skin and tendon reflexes exaggerated, no clonus, no Babinski; sphincters normal; no sensory defect except deafness.

Case 3. Male, aged thirty-seven. Brought into hospital in coma, not arousable. Two weeks before had had severe headache for a few hours. This recurred after ten days; after two or more days he vomited and sank into coma, with some sort of convulsion.

Examination. Deep coma; pupils, no light reaction; movements of resistance with moaning when disturbed; no paralysis; muscles held slightly contracted; tendon reflexes exaggerated, no clonus, no Babinski; sphincters acted reflexly.

Wassermann test of blood: at first positive, two days later, negative. Spinal fluid Wassermann, positive, ++++; polycytosis, culture negative. Died four days after coma began, necropsy not allowed.

Remarks. In all of these patients (Cases 1, 2, and 3) the possibility of encephalitis epidemica is kept in view. A syphilitic may of course have that infection. But syphilis of the base of the brain can produce coma before cranial nerve palsies occur. This may be due to interference with the basal arteries, causing cerebral ischemia; or with the veins, causing edema.

C. Infiltration into Meninges and Parenchyma of Spinal Cord (Meningo-Myelitis)

The brain and spinal cord receive their blood supply from arteries that run in the membranes, small branches from which run radially into the nervous tissues. These small branches are easily closed by pressure of infiltrations, or by distortion when the membranes are drawn tense. Thus result atrophy or softening according to whether the ischemia is gradual or sudden.

Case 4. Male, aged twenty-seven. Chancre in 1920. No secondaries. Wassermann test of blood now negative, of spinal fluid, positive, ++++, with much globulin. September 7, sudden numbness in lower limbs, followed by progressive paralysis in them, which was complete in five days; spastic bladder sphincter; pupillary light reaction shown; tendon and skin reflexes absent for ten days, then returned and were prompt; control of bladder returned; no sensory defect; power in lower limbs was returning. This is the so-called "Erb type of syphilitic spinal paralysis."

Case 5. Male, aged thirty-two. Much the same symptoms and findings as in Case 4; but this patient had a buzzing tinnitus indicating seventh nerve infiltration, also boring pains and numbness of the left limbs, exaggerated tendon jerks and a Babinski plantar reflex, indicating root involvement on the left side and more severe breakdown of the pyramidal fibers.

Case 6. Male aged twenty-seven. Clear syphilitic history, blood and spinal fluid Wassermann tests positive, ++++. On June 2, slight premonitory weakness in lower limbs. Then sudden loss of power in all limbs, diaphragm, face, palate,

pharynx, and larynx. Trismus was present. No loss of consciousness. Cheyne-Stokes respiration followed, then pneumonia.

Tendon jerks now exaggerated, clonus and Babinski present. Explosions of outward expressions of weeping or laughing on slight provocation. Under vigorous antisyphilitic treatment he recovered 50 per cent of the lost power.

Remarks. In Cases 4 and 5 the lesions were largely spinal, while the patient in Case 6 had a lesion involving the medulla oblongata and lower pons. In all three patients the pyramidal tracts were injured at the different levels respectively involved. In all three the motor nuclei suffered, but later showed considerable recovery. The lesions were probably thrombotic, but possibly due only to closure of vessels by pressure.

D. Degeneration of Afferent Tracts. Tabes Dorsalis. Pseudo-Tabes

Polyneuritis and the early root lesions of syphilis sometimes give symptoms indistinguishable from those of tabes dorsalis. The diagnosis is made when the former are cured by appropriate therapy. The degenerated tracts of true tabes cannot be restored.

Definition of Tabes Dorsalis. A syphilitic disease of the nervous system marked by degeneration of the afferent tracts with resulting characteristic pains, loss of pupillary light reflex and tendon reflexes, and often of co-ordinated muscle movements.

Those most commonly affected are the dorsal tracts of the spinal cord, then the optic tracts, less frequently the sensory tracts of the fifth, eighth, ninth, tenth, and eleventh cranial nerves.

The mechanism may be: (*a*) constriction of the root by newly-formed connective tissue; (*b*) selective action of a toxin to which the afferent tracts are sensitive.

Four cardinal symptoms are: shooting pains and crises, loss of tendon reflexes, irregularities in shape and reactions of pupils, and ataxia. Five other commonly found symptoms are: hypotonus of muscles, objective sensory defects, loss of sphincter control, loss of sexual feeling and reflexes, and trophic changes.

Case 7. Laboratory evidence positive; shooting pains five years, Argyll-Robertson pupils, no ataxia, tendon jerks lost, loss of sphincter control, loss of sexual feelings and capacity, objective sensory defects, vitiligo, and a Charcot knee-joint.

Case 8. Chancre five years ago, laboratory findings now negative; irregular pupils, partial Argyll-Robertson sign, loss of tendon jerks, loss of vibratory sense, loss of sexual feeling, vitiligo, and a Charcot knee-joint.

E. Destruction of the Brain Cortex. Paretic Dementia

Paretic dementia is a syphilitic disease of the nervous system marked primarily by atrophy of the cortical nerve-cells and in addition by more or less general nerve fiber and cell destruction throughout the nervous system.

The usual symptoms are: gradual reduction of the man to a vegetative automaton; irregular increase or decrease in tendon and skin reflexes, tremors, together with sensory and eye changes, such as mark tabes dorsalis.

Case. 9. History and laboratory findings of syphilis. Shooting pains, irregular pupils with Argyll-Robertson reflexes, tendon reflexes prompt in some parts, re-

duced in others, overexcitable sexually. Euphoria, loquacity, meddlesomeness, deterioration of judgment, and insomnia, are present.

Case 10. Aged thirty-seven. History and laboratory proofs of syphilis were positive. Argyll-Robertson pupils, blank face, coarse tremors, speech inarticulate, marked general ataxia, muscles feeble; exaggerated tendon reflexes, except right Achilles reflex, which was absent; Babinski present.

TREATMENT

The diagnosis must be made early and vigorous treatment started at once, otherwise permanent degenerations rapidly occur.

Intravenous salvarsan, 0.400 gram at first, increased to 0.700 or more. This may be continued every fifth day for six weeks, together with mercury. Its effectiveness should be checked by blood and spinal fluid tests at the end of each six weeks. A rest from treatment may then be allowed for from four to six weeks. This plan should be followed until symptoms and positive laboratory findings are absent, then less vigorous treatment should be given for two years.

Intraspinal treatment seems inadvisable for the following reasons:

1. Results thus far in patients who were not simultaneously receiving intravenous treatment do not show any verifiable advantage in the method.

2. The intraspinal dose is too small to produce results, being only ½ of 1 per cent of the ordinary dose as given intravenously.

3. Salvarsan given through the blood-stream reaches every living cell in the parenchyma of the nervous system. The spinal fluid bathes only the external lining-cells of the membranes, and is rapidly drained back into the venous system. Medicine thrown into it cannot be expected to affect cells within the brain and spinal cord any more than medicines in the peritoneal fluid would affect a gumma of the liver.